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Attorney Docket No. **5371.31.US02**

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Sir:

Transmitted herewith for filing is the patent application of **Patricia D. Murphy, Marga B. White, Mark B. Rabin; Sheri J. Olson; Matthew Yoshikawa; Geoffrey M. Jackson; Tara Eskandari; Brenda Schryer; and Michael Park** for **NOVEL CODING SEQUENCE HAPLOTYPES OF THE HUMAN BRCA2 GENE.**

Also, enclosed are:

1. Cover Sheet of Application;
2. 13 sheets of drawings;
3. Executed Declaration (2 sets);
4. Executed Small Entity Statement;
5. Assignment Cover Sheet;
6. Executed Assignment (2 sets);
7. Sequence Listing on Disk; and
5. Two (2) return postcards.

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Date **May 22, 1998**

Albert P. Halluin (Reg. No.25,227)

PTO/SB/05 (2/98)

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UTILITY PATENT APPLICATION TRANSMITTAL

(for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	5371.31.US02
First Named Inventor or Application Identifier	Patricia D. Murphy
Title	Novel Coding Sequence Haplotypes of the Human BRCA2 Gene
Express Mail Label No.	EM555262526US

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents

ADDRESS TO: Assistant Commissioner for Patents
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Washington, DC 20231

1. [X] *Fee Transmittal Form (Form PTO-1082) *(Submit an original and a duplicate for fee processing)*
2. [X] Specification [*Total Pages* 204] *(preferred arrangement set forth below)*
   - Descriptive title of the Invention
   - Cross References to Related Applications
   - Statement Regarding Fed sponsored R&D
   - Reference to Microfiche Appendix
   - Background of the Invention
   - Brief Summary of the Invention
   - Brief Description of the Drawings (if filed)
   - Detailed Description
   - Claims
   - Abstract of the Disclosure
3. [X] Drawing(s) *(35 USC 113)* [*Total Sheets* 13]
4. Oath or Declaration [*Total Pages* 6]
   - a. [X] Newly executed (original or copy)
   - b. [ ] Copy from a prior application (37 CFR 1.63(d)) *(for continuation/divisional with Box 17 completed)* ***[Note Box 5 below]***
     - i. [ ] DELETION OF INVENTOR(S) Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b)
5. [ ] Incorporation By Reference *(useable if Box 4b is checked)* The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 4b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.
6. [ ] Microfiche Computer Program *(Appendix)*
7. Nucleotide and/or Amino Acid Sequence Submission *(if applicable, all necessary)*
   - a. [X] Computer Readable Copy
   - b. [X] Paper Copy (identical to computer copy)
   - c. [ ] Statement verifying identity of above copies

ACCOMPANYING APPLICATION PARTS

8. [X] Assignment Papers (cover sheet & document(s))
9. [ ] 37 CFR 3.73(b) Statement *(when there is an assignee)* [ ] Power of Attorney
10. [ ] English Translation Document *(if applicable)*
11. [ ] Information Disclosure Statement (IDS)/PTO-1449 [ ] Copies of IDS Citations
12. [ ] Preliminary Amendment
13. [X] Return Receipt Postcard (MPEP 503) (Two) *(should be specifically itemized)*
14. [X] *Small Entity Statement(s) [ ] Statement filed in prior application, Status still proper and desired
15. [ ] Certified Copy of Priority Document(s) *(if foreign priority is claimed)*
16. [ ] Other:

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17. **If a CONTINUING APPLICATION**, *check appropriate box and supply the requisite information:*
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    Prior Application Information: Examiner: Group/Art Unit:

18. CORRESPONDENCE ADDRESS

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APPLICATION IN

THE UNITED STATES PATENT AND TRADEMARK OFFICE

FOR

NOVEL CODING SEQUENCE HAPLOTYPES OF THE HUMAN BRCA2 GENE

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NOVEL CODING SEQUENCE HAPLOTYPES OF THE HUMAN BRCA2 GENE

This is an U.S. utility patent application based on U.S. Provisional Application Serial Nos. 60/055,784 filed on August 15, 1997, 60/064,926 filed on November 7, 1997, and 60/065,367 filed on November 12, 1997.

FIELD OF THE INVENTION

This invention relates to a gene which has been associated with breast cancer where the gene is found to be mutated. More specifically, this invention relates to five unique coding sequences of BRCA2 gene $BRCA2^{(omi1)}$, $BRCA2^{(omi2)}$, $BRCA2^{(omi3)}$, $BRCA2^{(omi4)}$, and $BRCA2^{(omi5)}$ identified in human subjects which define five novel haplotypes.

BACKGROUND OF THE INVENTION

It has been estimated that about 5-10% of breast cancer is inherited (Rowell, S., *et al., American Journal of Human Genetics* 55:861-865 (1994)). The first gene associated with both breast and ovarian cancer was cloned in 1994 from chromosome 17 by Miki, Y., *et al., Science* 266:66-71 (1994). A second high-risk breast cancer conferring gene was located on chromosome 13 in 1994 (Wooster, R., *et al., Science* 265:2088-2090) and subsequently cloned in 1995 (Wooster, R., *et al., Nature* 378:789-792). Mutations in this "tumor suppressor" gene are thought to account for roughly 35% of inherited breast cancer and 80-90% of families with male breast cancer.

Locating one or more mutations in the BRCA2 region of chromosome 13 provides a promising approach to reducing the high incidence and mortality associated with breast cancer through the early detection of women and men at high risk. These individuals, once identified, can be targeted for more aggressive prevention programs. Screening is carried out by a variety of methods which include karyotyping, probe binding and DNA sequencing.

In DNA sequencing technology, genomic DNA is extracted from whole blood and the coding regions of the BRCA2 gene are amplified. Each of the coding regions may be sequenced completely and the results are compared to the normal DNA sequence of the gene. Alternatively, the coding sequence of the sample gene may be compared to a panel of known mutations or other screening procedure

before completely sequencing the gene and comparing it to a normal sequence of the gene.

The BRCA2 gene is divided into 27 separate exons. Exon 1 is noncoding, in that it is not part of the final functional BRCA2 protein product. The BRCA2 coding region spans roughly 10433 base pairs (bp) over 70 kb. Each exon consists of 100-600 bp, except for exons 10, 11 and 27. The full length mRNA is 11-12 kb. To sequence the coding region of the BRCA2 gene, each exon is amplified separately and the resulting PCR products are sequenced in the forward and reverse directions. Because exons 10, 11, and 27 are so large, we have divided them into three, twenty-one, and two overlapping PCR fragments (respectively) of approximately 250-625 bp each (segments "A" through "C" of exon 10, "A" through "U" of exon 11, and "A" through "B" of exon 27).

Many mutations and normal polymorphisms have already been reported in the BRCA2 gene. A world wide web site has been built to facilitate the detection and characterization of alterations in breast cancer susceptibility genes. Such mutations in BRCA2 can be accessed through the Breast Cancer Information Core (BIC) at http://www.nhgri.nih.gov/Intramural_research/Lab_transfer/Bic. This data site became publicly available on November 1, 1995. Friend, S. *et al. Nature Genetics* 11:238, (1995). The information on BRCA2 was added in February, 1996.

The genetics of Breast Cancer Syndrome is autosomal dominant with reduced penetrance. In simple terms, this means that the syndrome runs through families: (1) both sexes can be carriers (mostly women get the disease but men can both pass it on and occasionally get breast cancer); (2) most generations will likely have breast cancer; (3) occasionally women carriers either die young before they have the time to manifest disease (and yet have offspring who get it) or they never develop breast or ovarian cancer and die of old age (the latter people are said to have "reduced penetrance" because they never develop cancer). Pedigree analysis and genetic counseling is absolutely essential to the proper workup of a family prior to any lab work.

Until now, the only sources of genomic sequence information for BRCA2 were GenBank (Accession Number U43746), or through the Breast Information Core (BIC) database on the Internet which requires membership in the BIC consortium. However, based upon the disclosure of this patent application, in neither GenBank

nor BIC were the sequences identified and listed entirely accurate. There is a need in the art to correct these mistakes which otherwise may lead to misinterpretation of the sequence data from the patient as abnormal when it was not, or vice versa.

In addition, there is a need in the art to have available a functional allele profile which represents the most likely BRCA2 sequences to be found in the majority of the normal population. This functional allele profile is based upon frequent polymorphisms and the correct backbone sequence. The knowledge of several common normal haplotypes will make it possible for true mutations to be easily identified or differentiated from polymorphisms. Identification of mutations of the BRCA2 gene and protein would allow more widespread diagnostic screening for hereditary breast cancer than is currently possible.

The use of these common normal haplotypes, in addition to the previously published BRCA2 sequence, will reduce the likelihood of misinterpreting a "sequence variation" found in the normal population with a pathologic "mutation" (i.e. causes disease in the individual or puts the individual at a high risk of developing the disease). With large interest in breast cancer predisposition testing, misinterpretation is particularly worrisome. People who already have breast cancer are asking the clinical question: "is my disease caused by a heritable genetic mutation?" The relatives of the those with breast cancer are asking the question: "Am I also a carrier of the mutation my relative has? Thus, is my risk increased, and should I undergo a more aggressive surveillance program?"

SUMMARY OF THE INVENTION

The present invention is based on the discovery of the correct genomic BRCA2 sequence and five novel sequence haplotypes found in normal human subjects of the BRCA2 gene.

It is an object of this invention to provide the correct intronic/exonic sequence of the BRCA2 gene.

It is another object of this invention to provide five unique haplotype sequences of the BRCA2 gene in normal individuals which do not correspond to increased cancer susceptibility.

It is another object of this invention to sequence a BRCA2 gene or a portion thereof and compare it to the five haplotype sequences to determine whether a

sequence variation noted represents a polymorphism or a potentially harmful mutation.

It is another object of this invention to provide a list of the pairs which occur at each of ten polymorphic points in the BRCA2 gene.

It is another object of this invention to provide the rates of occurrence for the polymorphisms at codons 289, 372, 455, 743, 894, 991, 1132, 1269, 2414, and 2951 in the BRCA2 gene.

It is another object of this invention to provide a method wherein all exons of BRCA2 gene or parts thereof, are amplified with one or more oligonucleotide primers.

It is another object of this invention to provide a method of identifying a individual who carries no mutation(s) of the BRCA2 gene and is therefore at no increased risk or susceptibility to breast or ovarian cancer based on a finding that the individual does not carry an abnormal BRCA2 genes.

It is another object of this invention to provide a method of identifying a mutation in BRCA2 gene leading to predisposition or higher susceptibility to breast or ovarian cancer.

It is another object of this invention to provide five novel BRCA2 protein sequences derived from five BRCA2 haplotype sequences.

It is another object of the invention to encompass prokaryotic or eukaryotic host cells comprising an expression vector having a DNA sequence that encodes for all or a fragment of the five novel BRCA2 protein sequences, a BRCA2 polypeptide thereof, or a functional equivalent thereof.

It is another object of the invention to encompass an anti-BRCA2 protein antibody using all of fragments of the five novel BRCA2 protein sequences, a BRCA2 polypeptide thereof or a functional equivalent thereof as an immunogen.

There is a need in the art for cDNA sequences of the BRCA2 gene and for the protein sequences of BRCA2 gene from normal individuals who are not at risk for increased susceptibility for cancer. In order to determine whether a sample from a patient suspected of containing a BRCA2 mutation actually has the mutation, the patient's BRCA2 DNA and/or amino acid sequence need to be compared to all known normal BRCA2 sequences. Failure to compare the sequence obtained to all

naturally occurring normal sequences may result in reporting a sample as containing a potentially harmful mutation when it is a polymorphism without clinical significance.

A person skilled in the art of genetic susceptibility testing will find the present invention useful for:

a) identifying individuals having a normal BRCA2 gene with no coding sequence mutations, who therefore cannot be said to have an increased genetic susceptibility to breast or ovarian cancer from their BRCA2 genes;

b) avoiding misinterpretation of normal polymorphisms found in the BRCA2 gene;

c) determining the presence of a previously unknown mutation in the BRCA2 gene;

d) identifying a mutation in exon 11 of BRCA2 which indicates a predisposition or higher susceptibility to ovarian cancer than breast cancer (i.e., resides in the putative "ovarian cancer cluster" region);

e) probing a human sample of the BRCA2 gene by allele to determine the presence or absence of either polymorphic alleles or mutations;

f) performing gene therapy with the correct BRCA2 gene sequence.

g) performing protein replacement therapy with the correct BRCA 2 protein sequence or a functional equivalent thereof.

BRIEF DESCRIPTION OF THE FIGURES

FIGURE 1 shows the GenBank genomic sequence of BRCA2 (Accession Number U43746). The lower case letters denote intronic sequences and the upper case letters denote exonic sequences. Incorrect exonic sequences at exons 5 and 16 are shown with boldface type.

FIGURE 2 shows the corrected genomic sequence of BRCA2. The lower case letters denote intronic sequences and the upper case letters denote exonic sequences. Corrected intronic and exonic sequences at exons 5, 11 and 15 are shown with boldface type.

FIGURE 3 shows the alternative alleles at polymorphic sites along a chromosome which can be represented as a unit or "haplotype" within a gene such as BRCA2.

The haplotype that is in GenBank (GB) is shown with light shading. Five additional haplotypes are shown in FIGURE 3 (encompassing the alternative alleles found at nucleotide sites 1093, 1342, 1593, 2457, 2908, 3199, 3624, 4035, 7470 and 9079). BRCA2 $^{(omi\text{-}1)}$, BRCA2 $^{(omi\text{-}2)}$, BRCA2 $^{(omi\text{-}3)}$, BRCA2 $^{(omi\text{-}4)}$, and BRCA2 $^{(omi\text{-}5)}$ are represented with mixed dark and light shading (numbers 2, 4, 6, 8 and 10 from left to right). In total, 5 of 10 haplotypes along the BRCA2 gene are unique.

DETAILED DESCRIPTION OF THE INVENTION

DEFINITIONS

The following definitions are provided for the purpose of understanding this invention.

"Breast and Ovarian cancer" is understood by those skilled in the art to include breast, ovarian and pancreatic cancer in women and also breast, prostate and pancreatic cancer in men. BRCA2 is associated with genetic susceptibility to breast, ovarian and pancreatic cancer. Therefore, claims in this document which recite breast and/or ovarian cancer refer to breast, ovarian, prostate, and pancreatic cancers in men and women.

"Coding sequence" refers to those portions of a gene which, taken together, code for a peptide (protein), or which nucleic acid itself has function.

"Protein" or "peptide" refers to a sequence of amino acids which has function.

"BRCA2$^{(omi)}$" refers to the genomic BRCA2 sequence disclosed in Genbank (Accession Number U43746) wherein,

(1) a 10 bp stretch (5'-TTTATTTTAG-3') is intronic at 3' end of intron 4, rather than at the 5' end of exon 5; and

(2) a 16 bp stretch (5'-GTGTTCTCATAAACAG-3') is exonic at the 3' end of exon 15, rather than at the 5' end of exon.

"BRCA2$^{(omi\ 1\text{-}5)}$" refers to five unique DNA sequences of the BRCA2 gene and their introns (particularly the slice sites adjacent to the exons). These sequences were found by end to end sequencing of the BRCA2 gene from 5 individuals randomly drawn from the population and who were documented to have no family history of breast or ovarian cancer. The sequenced exons were found not to contain any truncating mutations. In all cases the change of a nucleic acid at a

polymorphic site lead to a codon change and a change of amino acid from the previously published standard in GenBank (see TABLE III). In some cases the frequency of occurrence of a nucleic acid change was found to differ from the published frequency or was newly determined. These sequence variations are believed to be alleles whose haplotypes do not indicate an increased risk for cancer.

"Normal DNA sequence" also called " normal gene sequence" refers to a nucleic acid sequence, the nucleic acid of which are known to occur at their respective positions with high frequency in a population of individuals who carry the gene which codes for a normally functioning protein, or which itself has normal function.

"Normal Protein Sequence" refers to the protein sequence, the amino acids of which are known to occur with high frequency in a population of individuals who carry the gene which codes for a normally functioning protein.

"Normal Sequence" refers to the nucleic acid or protein sequence, the nucleic or amino acids of which are known to occur with high frequency in a population of individuals who carry the gene which codes for a normally functioning protein, or which nucleic acid itself has a normal function.

"Haplotype" refers to a series of specific alleles within a gene along a chromosome.

"Functional allele profile" refers a list of those alleles in the normal population which have the funll function.

"Mutation" refers to a base change or a gain or loss of base pair(s) in a DNA sequence, which results in a DNA sequence coding for a non-functional protein or a protein with substantially reduced or altered function.

"Polymorphism" refers to a base change in a DNA sequence which is not associated with known pathology.

"Primer" refers to a sequence comprising about 15 or more nucleotides having a sequence complementary to the BRCA2 gene. Other primers which can be used for primer hybridization will be known or readily ascertainable to those skilled in the art.

"Substantially complementary to" refers to primer sequences which hybridize to the sequences provided under stringent conditions and/or sequences having

sufficient homology with BRCA2 sequences, such that the allele specific oligonucleotide primers hybridize to the BRCA2 sequences to which they are complimentary.

"Isolated nucleic acids" refers to nucleic acids substantially free of other nucleic acids, proteins, lipids, carbohydrates or other materials with which they may be associated. Such association is typically either in cellular material or in a synthesis medium.

"Biological sample" or "body sample" refers to a sample containing DNA oatained from a biological source. The sample may be from a living, dead or even archeological source from a variety of tissues and cells. Examples include body fluid (e.g. blood (leukocytes), urine (epithelial cells), saliva, breast milk, menstrual flow, cervical and vaginal secretions, etc.), skin, hair roots/follicle, mucus membrane (e.g. buccal or tongue cell scrapings), cervicovaginal cells (from PAP smear, etc.), lymphatic tissue, internal tissue (normal or tumor).

"Vector" refers to any polynucleotide which is capable of self replication or inducing integration into a self-replicating polynucleotide. Examples include polynucleotides containing an origin or replication or an integration site. Vectors may be intergrated into the host cell's chromosome or form an autonomously replicating unit.

"A tumor growth inhibitor" refers to a molecule such as, all or a fragment of BRCA2 protein, a BRCA2 polypeptide, or a functional equivalent thereof that is effective for preventing the formation of, reducing, or eliminating a transformed or malignant phenotype of breast or ovarian cancer cells.

"A BRCA2 polypeptide" refers to a BRCA2 polypeptide either directly derived from the BRCA2 protein, or homologous to the BRCA2 protein, or a fusion protein consisting of all or fragments of the BRCA2 protein and polypeptides.

"A functional equivalent" refers to a molecule including an unnatural BRCA2 polypeptide, a drug or a natural product which retains substantial biological activity as the native BRCA2 protein. The activity and function of BRCA2 protein may include transactivation, granin, DNA repair, among others.

"A target polynucleotide" refers to the nucleic acid sequence of interest, for example, the BRCA2 encoding polynucleotide. Other primers which can be used for primer hybridization will be known or readily ascertainable to those of skill in the art.

The invention in several of its embodiments includes: an isolated DNA sequence of the BRCA2 coding sequence as set forth in SEQ ID NO:4, 6, 8, 10, and 12, a protein sequence of the BRCA2 protein as set forth in SEQ ID NO:5, 7, 9, 11, 13, a method of identifying individuals having a normal BRCA2 gene with no increased risk for breast and ovarian cancer, a method of detecting an increased genetic susceptibility to breast and ovarian cancer in an individual resulting from the presence of a mutation in the BRCA2 coding sequence, a method of performing gene therapy to prevent or treat a tumor, a method of protein replacement therapy to prevent or treat a tumor, a diagnostic reagent comprising all or fragments of the disclosed BRCA2 cDNA and protein sequences.

SEQUENCING

Any nucleic acid specimen, in purified or non-purified form, can be utilized as the starting nucleic acid, providing it contains, or is suspected of containing, the specific nucleic acid sequence containing a polymorphic or a mutant allele. Thus, the process may amplify, for example, DNA or RNA, including mRNA and cDNA, wherein DNA or RNA may be single stranded or double stranded. In the event that RNA is to be used as a template, enzymes and/or conditions optimal for reverse transcribing the template to DNA would be utilized. In addition, a DNA-RNA hybrid which contains one strand of each may be utilized. A mixture of nucleic acids may also be employed, or the nucleic acids produced in a previous method such as an amplification reaction using the same or different primers may be so utilized. The specific nucleic acid sequence to be amplified, *i.e.,* the polymorphic and/or the mutant allele, may be a fraction of a larger molecule or can be present initially as a discrete molecule, so that the specific sequence constitutes the entire nucleic acid. A variety of amplification techniques may be used such as ligating the DNA sample or fragments thereof to a vector capable of replication or incorporation into a replicating system thereby increasing the number of copies of DNA suspected of containing at least a portion of the BRCA2 gene. Amplification techniques include so called "shot gun cloning". It is not necessary that the sequence to be amplified be present initially in a pure form; it may be a minor fraction of a complex mixture, such as contained in whole human DNA.

It should be noted that one need not sequence the entire coding region or even an entire DNA fragment in order to determine whether or not a mutation is present. For example, when a mutation is known in one family member, it is sufficient to determine the sequence at only the mutation site by sequencing or by other mutation detection systems such as ASO when testing other family members.

DNA utilized herein may be extracted from a body sample, such as blood, tissue material and other biological sample by a variety of techniques such as that described by Maniatis, *et al.* in *Molecular Cloning: A Laboratory Manual,* Cold Spring Harbor, NY, p 280-281, 1982). If the extracted sample is impure, it may be treated before amplification with an amount of a reagent effective to open the cells, and to expose and/or separate the strand(s) of the nucleic acid(s). This lysing and nucleic acid denaturing step to expose and separate the strands will allow amplification to occur much more readily.

For amplification by cloning, the isolated DNA may be cleaved into fragments by a restriction endonuclease or by shearing by passing the DNA containing mixture through a 25 gauge needle from a syringe to prepare 1-1.5 kb fragments. The fragments are then ligated to a cleaved vector (virus, plasmid, transposon, cosmid etc.) and then the recombinant vector so formed is then replicated in a manner typical for that vector.

For a PCR amplification, the deoxyribonucleotide triphosphates dATP, dCTP, dGTP, and dTTP are added to the synthesis mixture, either separately or together with the primers, in adequate amounts and the resulting solution is heated to about 90°-100°C from about 1 to 10 minutes, preferably from 1 to 4 minutes. After this heating period, the solution is allowed to cool, which is preferable for the primer hybridization. To the cooled mixture is added an appropriate agent for effecting the primer extension reaction (called herein "agent for polymerization"), and the reaction is allowed to occur under conditions known in the art. The agent for polymerization may also be added together with the other reagents if it is heat stable. This synthesis (or amplification) reaction may occur at room temperature up to a temperature above which the agent for polymerization no longer functions. Thus, for example, if DNA polymerase is used as the agent, the temperature is generally no greater than about 40°C. Most conveniently the reaction occurs at

room temperature. When using thermostable DNA polymerase such as Taq, higher temperature may be used.

The allele specific oligonucleotide primers are useful in determining whether a subject is at risk of having breast or ovarian cancer, and also useful for characterizing a tumor. Primers direct amplification of a target polynucleotide prior to sequencing. These unique BRCA2 oligonucleotide primers for exons 2-27 shown in TABLE II were designed and produced specifically to optimize amplification of portions of BRCA2 which are to be sequenced.

The primers used to carry out this invention embrace oligonucleotides of sufficient length and appropriate sequence to provide initiation of polymerization. Environmental conditions conducive to synthesis include the presence of nucleoside triphosphates and an agent for polymerization, such as DNA polymerase, and a suitable temperature and pH. The primer is preferably single stranded for maximum efficiency in amplification, but may be double stranded. If double stranded, the primer is first treated to separate its strands before being used to prepare extension products. The primer must be sufficiently long to prime the synthesis of extension products in the presence of the inducing agent for polymerization. The exact length of primer will depend on many factors, including temperature, buffer, and nucleotide composition. The oligonucleotide primer typically contains 18-28 bp plus in some cases an M13 "tail" for convenience.

Primers used to carry out this invention are designed to be substantially complementary to each strand of the genomic locus to be amplified. This means that the primers must be sufficiently complementary to hybridize with their respective strands under conditions which allow the agent for polymerization to perform. In other words, the primers should have sufficient complementarity with the 5' and 3' sequences flanking the mutation to hybridize therewith and permit amplification of the genomic locus.

Oligonucleotide primers of the invention are employed in the amplification process which is an enzymatic chain reaction that produces exponential quantities of polymorphic locus relative to the number of reaction steps involved. Typically, one primer is complementary to the negative (-) strand of the polymorphic locus and the other is complementary to the positive (+) strand. Annealing the primers to denatured nucleic acid followed by extension with an enzyme, such as the large

fragment of DNA polymerase I (Klenow) and nucleotides, results in newly synthesized + and - strands containing the target polymorphic locus sequence. Because these newly synthesized sequences are also templates, repeated cycles of denaturing, primer annealing, and extension results in exponential production of the region (*i.e.,* the target polymorphic locus sequence) defined by the primers. The product of the chain reaction is a discreet nucleic acid duplex with termini corresponding to the ends of the specific primers employed.

The oligonucleotide primers of the invention may be prepared using any suitable method, such as conventional phosphotriester and phosphodiester methods or automated embodiments thereof. In one such automated embodiment, diethylphosphoramidites are used as starting materials and may be synthesized as described by Beaucage, *et al.*, *Tetrahedron Letters*, 22:1859-1862, 1981. One method for synthesizing oligonucleotides on a modified solid support is described in U.S. Patent No. 4,458,066.

The agent for polymerization may be any compound or system which will function to accomplish the synthesis of primer extension products, including enzymes. Suitable enzymes for this purpose include, for example, *E. coli* DNA polymerase I, Klenow fragment of *E. coli* DNA polymerase, polymerase muteins, reverse transcriptase, other enzymes, including heat-stable enzymes (*i.e.,* those enzymes which perform primer extension after being subjected to temperatures sufficiently elevated to cause denaturation), such as *Taq* polymerase. Suitable enzymes will facilitate combination of the nucleotides in the proper manner to form the primer extension products which are complementary to each polymorphic locus nucleic acid strand. Generally, the synthesis will be initiated at the 3' end of each primer and proceed in the 5' direction along the template strand, until synthesis terminates, producing molecules of different lengths.

The newly synthesized strand and its complementary nucleic acid strand will form a double-stranded molecule under hybridizing conditions described above and this hybrid is used in subsequent steps of the process. In the next step, the newly synthesized double-stranded molecule is subjected to denaturing conditions using any of the procedures described above to provide single-stranded molecules.

The steps of denaturing, annealing, and extension product synthesis can be repeated as often as needed to amplify the target polymorphic locus nucleic acid

sequence to the extent necessary for detection. The amount of the specific nucleic acid sequence produced will accumulate in an exponential fashion. Amplification is described in *PCR. A Practical Approach*, ILR Press, Eds. M. J. McPherson, P. Quirke, and G. R. Taylor, 1992.

The amplification products may be detected by Southern blots analysis, without using radioactive probes. In such a process, for example, a small sample of DNA containing a very low level of the nucleic acid sequence of the polymorphic locus is amplified, and analyzed via a Southern blotting technique or similarly, using dot blot analysis. The use of non-radioactive probes or labels is facilitated by the high level of the amplified signal. Alternatively, probes used to detect the amplified products can be directly or indirectly detectably labeled, for example, with a radioisotope, a fluorescent compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator or an enzyme. Those of ordinary skill in the art will know of other suitable labels for binding to the probe, or will be able to ascertain such, using routine experimentation.

Sequences amplified by the methods of the invention can be further evaluated, detected, cloned, sequenced, and the like, either in solution or after binding to a solid support, by any method usually applied to the detection of a specific DNA sequence such as PCR, oligomer restriction (Saiki, *et.al.*, *Bio/Technology*, 3:1008-1012, 1985), allele-specific oligonucleotide (ASO) probe analysis (Conner, *et al., Proc. Natl. Acad. Sci.* U.S.A., 80:278, 1983), oligonucleotide ligation assays (OLAs) (Landgren, *et al., Science,* 241:1007, 1988), and the like. Molecular techniques for DNA analysis have been reviewed (Landgren, *et al., Science*, 242:229-237, 1988).

Preferably, the method of amplifying is by PCR, as described herein and as is commonly used by those of ordinary skill in the art. Alternative methods of amplification have been described and can also be employed as long as the BRCA2 locus amplified by PCR using primers of the invention is similarly amplified by the alternative means. Such alternative amplification systems include but are not limited to self-sustained sequence replication, which begins with a short sequence of RNA of interest and a T7 promoter. Reverse transcriptase copies the RNA into cDNA and degrades the RNA, followed by reverse transcriptase polymerizing a second strand of DNA. Another nucleic acid amplification technique

is nucleic acid sequence-based amplification (NASBA) which uses reverse transcription and T7 RNA polymerase and incorporates two primers to target its cycling scheme. NASBA can begin with either DNA or RNA and finish with either, and amplifies to 10^8 copies within 60 to 90 minutes. Alternatively, nucleic acid can be amplified by ligation activated transcription (LAT). LAT works from a single-stranded template with a single primer that is partially single-stranded and partially double-stranded. Amplification is initiated by ligating a cDNA to the promoter oligonucleotide and within a few hours, and amplification is 10^8 to 10^9 fold. Another amplification system useful in the method of the invention is the Qβ Replicase System. The Qβ replicase system can be utilized by attaching an RNA sequence called MDV-1 to RNA complementary to a DNA sequence of interest. Upon mixing with a sample, the hybrid RNA finds its complement among the specimen's mRNAs and binds, activating the replicase to copy the tag-along sequence of interest. Another nucleic acid amplification technique, ligase chain reaction (LCR), works by using two differently labeled halves of a sequence of interest which are covalently bonded by ligase in the presence of the contiguous sequence in a sample, forming a new target. The repair chain reaction (RCR) nucleic acid amplification technique uses two complementary and target-specific oligonucleotide probe pairs, thermostable polymerase and ligase, and DNA nucleotides to geometrically amplify targeted sequences. A 2-base gap separates the oligonucleotide probe pairs, and the RCR fills and joins the gap, mimicking normal DNA repair. Nucleic acid amplification by strand displacement activation (SDA) utilizes a short primer containing a recognition site for *hincII* with short overhang on the 5' end which binds to target DNA. A DNA polymerase fills in the part of the primer opposite the overhang with sulfur-containing adenine analogs. *HincII* is added but only cuts the unmodified DNA strand. A DNA polymerase that lacks 5' exonuclease activity enters at the site of the nick and begins to polymerize, displacing the initial primer strand downstream and building a new one which serves as more primer. SDA produces greater than 10^7-fold amplification in 2 hours at 37°C. Unlike PCR and LCR, SDA does not require instrumented Temperature cycling.

Another method is a process for amplifying nucleic acid sequences from a DNA or RNA template which may be purified or may exist in a mixture of nucleic acids. The resulting nucleic acid sequences may be exact copies of the template, or may be modified. The process has advantages over PCR in that it increases the fidelity of copying a specific nucleic acid sequence, and it allows one to more efficiently detect a particular point mutation in a single assay. A target nucleic acid is amplified enzymatically while avoiding strand displacement. Three primers are used. A first primer is complementary to the first end of the target. A second primer is complementary to the second end of the target. A third primer which is similar to the first end of the target and which is substantially complementary to at least a portion of the first primer such that when the third primer is hybridized to the first primer, the position of the third primer complementary to the base at the 5' end of the first primer contains a modification which substantially avoids strand displacement. This method is detailed in U.S. Patent 5,593,840 to Bhatnagar et al. 1997, incorporated herein by reference.

Finally, recent application of DNA chips or microarray technology where DNA or oligonucleotides are immobilized on small solid support may also be used to rapidly sequence sample BRCA2 gene and analyze its expression. Typically, high density arrays of DNA fragment are fabricated on glass or nylon substrates by *in situ* light-directed combinatorial synthesis or by conventional synthesis followed by immobilization (Fodor *et al.* U.S. patent No. 5,445,934). Sample DNA or RNA may be amplified by PCR, labeled with a fluorescent tag, and hybridized to the microarray. Examples of this technology are provided in U.S. Patents 5,510, 270, U.S. 5,547,839, incorporated herein by reference.

All exonic and adjacent intronic sequences of the BRCA2 gene were obtained by end to end sequencing of five normal subjects in the manner described above followed by analysis of the data obtained. The data obtained provided us with the opportunity to establish the correct intronic/exonic structure of the BRCA2 gene. In addition, we evaluated six previously published normal polymorphisms (1342, 2457, 3199, 3624, 4035, and 7470) for correctness and frequency in the population, and to identify four additional polymorphisms not previously characterized (1093, 1593, 2908, and 9079).

GENE THERAPY

The polynucleotide(s) which result from either sense or antisense transcription of any exon or the entire coding sequence or fragments of BRCA2 gene may be used for gene therapy. A variety of methods are known for gene transfer, any of which might be available for use.

Direct injection of Recombinant DNA in vivo:

1. Direct injection of "naked" DNA directly with a syringe and needle into a specific tissue, infused through a vascular bed, or transferred through a catheter into endothelial cells.

2. Direct injection of DNA that is contained in artificially generated lipid vesicles or other encapsulating vehicles.

3. Direct injection of DNA conjugated to a target receptor structure, such as a diptheria toxin, an antibody or other suitable receptor.

4. Direct injection by particle bombardment. For example, the DNA may be coated onto gold particles and shot into the cells.

Human Artificial Chromosomes

The gene delivery approach involves the use of human chromosomes that have been stripped down to contain only the essential components for replication and the genes desired for transfer.

Receptor-Mediated Gene Transfer

DNA is linked to a targeting molecule that will bind to specific cell-surface receptors, inducing endocytosis and transfer of the DNA into mammalian cells. One such technique uses poly-L-lysine to link asialoglycoprotein to DNA. An adenovirus is also added to the complex to disrupt the lysosomes and thus allow the DNA to avoid degradation and move to the nucleus. Infusion of these particles intravenously has resulted in gene transfer into hepatocytes.

RECOMBINANT VIRUS VECTORS

Several vectors may be used in gene therapy. Among them are the Moloney Murine Leukemia Virus (MoMLV) Vectors, the adenovirus vectors, the Adeno-Associated Virus (AAV) vectors, the herpes simplex virus (HSV) vectors, the poxvirus vectors, the retrovirus vectors, and human immunodeficiency virus (HIV) vectors.

GENE REPLACEMENT AND REPAIR

The ideal genetic manipulation for treatment of a genetic disease would be the actual replacement of the defective gene with a normal copy of the gene. Homologous recombination is the term used for switching out a section of DNA and replacing it with a new piece. By this technique, the defective gene may be replaced with a normal gene which expresses a functioning BRCA2 tumor growth inhibitor protein.

A complete description of gene therapy can also be found in "Gene Therapy A Primer For Physicians" 2d Ed. by Kenneth W. Culver, M.D. Publ. Mary Ann Liebert Inc. (1996). Two Gene Therapy Protocols for BRCA1 gene have been approved by the Recombinant DNA Advisory Committee for Jeffrey T. Holt et al. They are listed as 9602-148, and 9603-149 and are available from the NIH. Protocols for BRCA2 gene therapy may be similarly employed. The isolated BRCA2 gene may be synthesized or constructed from amplification products and inserted into a vector such as the LXSN vector.

A BRCA2 POLYPEPTIDE OR ITS FUNCTIONAL EQUIVALENT

The growth of breast and ovarian cancer may be arrested or prevented by directly increasing the BRCA2 protein level where inadequate functional BRCA2 activity is responsible for breast and ovarian cancer. The cDNA and amino acid sequences of five novel BRCA2 haplotypes are disclosed herein (SEQ ID No:4-13). All or a fragment of BRCA2 protein may be used in therapeutic or prophylactic treatment of breast and ovarian cancer. Such a fragment may have a similar biological function as the native BRCA2 protein or may have a desired biological function as specified below. BRCA2 polypeptides or their functional equivalents including homologous and modified polypeptide sequences are also within the scope of the present invention. Changes in the native sequence may be advantageous in producing or using the BRCA2 derived polypeptides or functional equivalents suitable for therapeutic or prophylactic treatment of breast and ovarian cancer. For example, these changes may be desirable for producing resistance against *in vivo* proteolytic cleavage, for facilitating transportation and delivery of

therapeutic reagents, for localizing and compartmentalizing tumor suppressing agents, or for expression, isolating and purifying the target species.

There are a variety of methods to produce an active BRCA2 polypeptide or a functional equivalent as a tumor growth inhibitor. For example, one or more amino acids may be substituted, deleted, or inserted using methods well known in the art (Maniatis *et al.*, 1982). Considerations of polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphiphathic nature of the amino acids play an important role in designing homologous polypeptide changes suitable for the intended treatment. In particular, conservative amino acid substitution using amino acids that are related in side-chain structure and charge may be employed to preserve the chemical and biological property. A homologous polyeptide typically contains at least 70% homology to the native sequence. Unnatural forms of the polypeptide may also be incorporated so long as the modification retains substantial biological activity. These unnatural polypeptides typically include structural mimics and chemical medications, which have similar three-dimensional structures as the active regions of the native BRCA2 protein. For example, these modifications may include terminal D-amino acids, cyclic peptides, unnatural amino acids side chains, pseudopeptide bonds, N-terminal acetylation, glycosylation, and biotinylation, etc. These unnatural forms of polypeptide may have a desired biological function, for example, they may be particularly robust in the presence of cellular or serum proteases and exopeptidase. An effective BRCA2 polypeptide or a functional equivalent may also be recognized by the reduction of the native BRCA2 protein. Regions of the BRCA2 protein may be systematically deleted to identify which regions are essential for tumor growth inhibitor activity. These smaller fragments of BRCA2 protein may then be subjected to structural and functional modification to derive therapeutically or prophylactically effective regiments. Finally, drugs, natural products or small molecules may be screened or synthesized to mimic the function of the BRCA2 protein. Typically, the active species retain the essential three-dimensional shape and chemical reactivity, and therefore retain the desired aspects of the biological activity of the native BRCA2 protein. The activity and function of BRCA2 may include transactivation, granin, DNA repair among others. Functions of BRCA2 protein are also reviewed in Bertwistle and Ashworth, *Curr. Opin. Genet. Dev.* 8(1): 14-20 (1998) and Zhang *et al.*, *Cell* 92:433-436 (1998). It will be

apparent to one skilled in the art that a BRCA2 polypeptide or a functional equivalent may be selected because such polypeptide or functional equivalent possesses similar biological activity as the native BRCA2 protein.

EXPRESSION OF THE BRCA2 PROTEIN AND POLYPEPTIDE IN HOST CELLS

All or fragments of the BRCA2 protein and polypeptide may be produced by host cells that are capable of directing the replication and the expression of foreign genes. Suitable host cells include prokaryotes, yeast cells, or higher eukaryotic cells, which contain an expression vector comprising all or a fragment of the BRCA2 cDNA sequence (SEQ. ID No: 4, 6, 8, 10, or 12) operatively linked to one or more regulatory sequences to produce the intended BRCA2 protein or polypeptide. Prokaryotes may include gram negative or gram positive organisms, for example *E. coli* or *Bacillus* strains. Suitable eukaryotic host cells may include yeast, virus, and mamalian systems. For example, Sf9 insect cells and human cell lines, such as COS, MCF7, HeLa, 293T, HBL100, SW480, and HCT116 cells.

A broad variety of suitable expression vectors are available in the art. An expression vector typically contains an origin of replication, a promoter, a phenotypic selection gene (antibiotic resistance or autotrophic requirement), and a DNA sequence coding for all or fragments of the BRCA2 protein. The expression vectors may also include other operatively linked regulatory DNA sequences known in the art, for example, stability leader sequences, secretory leader sequences, restriction enzyme cleavage sequences, polyadenylation sequences, and termination sequences, among others. The essential and regulatory elements of the expression vector must be compatible with the intended host cell. Suitable expression vectors containing the desired coding and control regions may be constructed using standard recombinant DNA techniques known in the art, many of which are described in Sambrook, *et al.*, Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y. (1989). For example, suitable origins of replication may include Col E1, SV4O viral and M13 origins of replication. Suitable promoters may be constitutive or inducible, for example, tac promoter, lac Z promoter, SV40 promoter, MMTV promoter, and LXSN promoter. Examples of selectable markers include neomycin, ampicillin, and hygromycin resistance and the like. Many suitable prokaryotic, viral and mammalian

expression vectors may be obtained commercially, for example, from Invitrogen Corp., San Diego, CA or from Clontech, Palo Alto, CA. It may be desirable that the BRCA2 protein or polypeptide is produced as a fusion protein to enhance the expression in selected host cells, to detect the expression in transfected cells, or to simplify the purification process. Suitable fusion partners for the BRCA2 protein or polypeptide are well known in the art and may include β-galactosidase, glutathione-S-transferase, and poly-histidine tag.

Expression vectors may be introduced into host cells by various methods known in the art. The transformation procedure used depends upon the host to be transformed. Methods for introduction of vectors into host cells may include calcium phosphate precipitation, electrosporation, dextran-mediated transfection, liposome encapsulation, nucleus microinjection, and viral or phage infection, among others.

Once an expression vector has been introduced into a suitable host cell, the host cell may be cultured under conditions permitting expression of large amounts of the BRCA2 protein or polypeptide. The expression product may be identified by many approaches well known in the art, for example, sequencing after PCR-based amplification, hybridization using probes complementary to the desired DNA sequence, the presence or absence of marker gene functions such as enzyme activity or antibiotic resistance, the level of mRNA production encoding the intended sequence, immunological detection of a gene product using monoclonal and polyclonal antibodies, such as Western blotting or ELISA. The BRCA2 protein or polypeptides produced in this manner may then be isolated following cell lysis and purified using various protein purification techniques known in the art, for example, ion exchange chromatography, gel filtration chromatography and immunoaffinity chromatography.

It is generally preferred that whenever possible, longer fragments of BRCA2 protein or polypeptide are used, particularly to include the desired functional domains of BRCA2 protein. Expression of shorter fragments of DNA may be useful in generating BRCA2 derived immunogen for the production of anti-BRCA2 antibodies. It should, of course, be understood that not all expression vectors, DNA regulatory sequences or host cells will function equally well to express the BRCA2 protein or polypeptides of the present invention. However, one of ordinary skill in the art may make a selection among expression vectors, DNA regulatory

sequences, host cells, and codon usage in order to optimize expression using known technology in the art without undue experimentation. Studies of BRCA2 protein function and examples of genetic manipulation of BRCA2 protein are summarized in two recent review articles, Bertwistle and Ashworth, *Curr. Opin. Genet. Dev.* 8(1): 14-20 (1998) and Zhang *et al.*, *Cell* 92:433-436 (1998).

IN VITRO SYNTHESIS AND CHEMICAL SYNTHESIS

Although it is preferred that fragments of the BRCA2 protein or polypeptides be obtained by overexpression in prokaryotic or eukaryotic host cells, the BRCA2 polypeptides or their functional equivalents may also be obtained by *in vitro* translation or synthetic means by methods known to those of ordinary skill in the art. For example, *in vitro* translation may employ an mRNA encoded by a DNA sequence coding for fragments of the BRCA2 protein or polypeptides. Chemical synthesis methodology such as solid phase synthesis may be used to synthesize a BRCA2 polypeptide structural mimic and chemically modified analogs thereof. The polypeptides or the modifications and mimic thereof produced in this manner may then be isolated and purified using various purification techniques, such as chromatographic procedures including ion exchange chromatography, gel filtration chromatography and immunoaffinity chromatography.

PROTEIN REPLACEMENT THERAPY

The tumor suppressing function of BRCA2 suggests that various BRCA2 protein targeted therapies may be utilized in treating and preventing tumors in breast and ovarian cancer. The present invention therefore includes therapeutic and prophylactic treatment of breast and ovarian cancer using therapeutic pharmaceutical compositions containing the BRCA2 protein, polypeptides, or their functional equivalents. For example, protein replacement therapy may involve directly administering the BRCA2 protein, a BRCA2 polypeptide, or a functional equivalent in a pharmaceutically effective carrier. Alternatively, protein replacement therapy may utilize tumor antigen specific antibody fused to fragments of the BRCA2 protein, a polypeptide, or a functional equivalent to deliver anti-cancer regiments specifically to the tumor cells.

To prepare the pharmaceutical compositions of the present invention, an active BRCA2 protein, a BRCA2 polypeptide, or its functional equivalent is combined with a pharmaceutical carrier selected and prepared according to conventional pharmaceutical compounding techniques. A suitable amount of the composition may be administered locally to the site of a tumor or systemically to arrest the proliferation of tumor cells. The methods for administration, may include parenteral, oral, or intravenous, among others according to established protocols in the art.

Pharmaceutically acceptable solid or liquid carriers or components which may be added to enhance or stabilize the composition, or to facilitate preparation of the composition include, without limitation, syrup, water, isotonic solution, 5 % glucose in water or buffered sodium or ammonium acetate solution, oils, glycerin, alcohols, flavoring agents, preservatives, coloring agents, starches, sugars, diluents, granulating agents, lubricants, binders, and sustained release materials. The dosage at which the therapeutic compositions are administered may vary within a wide range and depends on various factors, such as the stage of cancer progression, the age and condition of the patient, and may be individually adjusted.

DIAGNOSTIC REAGENTS

The BRCA2 protein, polypeptides, their functional equivalents, antibodies, and polynucleotides may be used in a wide variety of ways in addition to gene therapy and protein replacement therapy. They may be useful as diagnostic reagents to measure normal or abnormal activity of BRCA2 at the DNA, RNA, and protein level. The present invention therefore encompasses the diagnostic reagents derived from the BRCA2 cDNA and protein sequences as set forth in SEQ. ID. Nos: 4-13. These reagents may be utilized in methods for monitoring disease progression, for determining patients suited for gene and protein replacement therapy, or for detecting the presence or quantifying the amount of a tumor growth inhibitor following such therapy. Such methods may involve conventional histochemical techniques, such as obtaining a tumor tissue from the patient, preparing an extract and testing this extract for tumor growth or metabolism. For example, the test for tumor growth may involve measuring abnormal BRCA2 activity using conventional diagnostic assays, such as Southern, Northern, and Western blotting, PCR, RT-PCR, and immunoprecipitation. In

biopsies of tumor tissues, the loss of BRCA2 expression in tumor tissue may be verified by RT-PCR and Northern blotting at the RNA level. A Southern blot analysis, genomic PCR, or fluorescence in situ hybridization (FISH) may also be performed to examine the mutations of BRCA2 at the DNA level. And, a Western blotting, protein truncation assay, or immunoprecipitation may be utilized to analysis the effect at the protein level.

These diagnostic reagents are typically either covalently or non convalently attached to a detectable label. Such a label includes a radioactive label, a colorimetric enzyme label, a fluorescence label, or an epitope label. Frequently, a reporter gene downstream of the regulatory sequences is fused with the BRCA2 protein or polypeptide to facilitate the detection and purification of the target species. Commonly used reporter genes in BRCA2 fusion proteins include β-galactosidase and luciferase gene.

The BRCA2 protein, polypeptides, their functional equivalents, antibodies, and polynucleotides may also be useful in the study of the characteristics of BRCA2 proteins, such as structure and function of BRCA2 in oncogenesis or subcellular localization of BRCA2 protein in normal and cancerous cell. For example, yeast two-hybrid system has been used in the study of cellular function of BRCA2 to identify the regulator and effector of BRCA2 tumor suppressing function (Sharan *et al.*, *Nature* 386:804-810 (1997) and Katagiri *et al., Genes, Chromosomes & Cancer* 21:217-222 (1988)). In addition, the BRCA2 protein, polypeptides, their functional equivalents, antibodies, and polynucleotides may also be used in *in vivo* cell based and *in vitro* cell free assays to screen natural products and synthetic compounds which may mimic, regulate or stimulate BRCA2 protein function.

ANTISENSE INHIBITION

Antisense suppression of endogenous BRCA2 expression may assess the effect of BRCA2 protein on cell growth inhibition using known method in the art (Crooke, *Annu. Rev. Pharmacol. Toxicol.* 32:329-376 (1992) and Robinson-Benion and Holt, *Methods Enzymol.* 254:363-375 (1995)). Given the cDNA sequence as set forth in SEQ ID. NO: 4, 6, 8, 10, and 12, one of skill in the art can readily obtain anti-sense strand of DNA and RNA sequences to interfere with the production of wild-type BRCA2 protein or the mutated form of BRCA2 protein. Alternatively,

antisense oligonucleotide may be designed to target the control sequences of BRCA2 gene to reduce or prevent the expression of the endogenous BRCA2 gene.

ANTIBODIES

The BRCA2 protein, polypeptides, or their functional equivalents may be used as immunogens to prepare polyclonal or monoclonal antibodies capable of binding the BRCA2 derived antigens in a known manner (Harlow & Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988). These antibodies may be used for the detection of the BRCA2 protein, polypeptides, or a functional equivalent in an immunoassay, such as ELISA, Western blot, radioimmunoassay, enzyme immunoassay, and immunocytochemistry. Typically, an anti-BRCA2 antibody is in solution or is attached to a solid surface such as a plate, a particle, a bead, or a tube. The antibody is allowed to contact a biological sample or a blot suspected of containing the BRCA2 protein or polypeptide to form a primary immunocomplex. After sufficient incubation period, the primary immunocomplex is washed to remove any non-specifically bound species. The amount of specifically bound BRCA2 protein or polypeptide may be determined using the detection of an attached label or a marker, such as a radioactive, a fluorescent, or an enzymatic label. Alternatively, the detection of BRCA2 derived antigen is allowed by forming a secondary immunocomplex using a second antibody which is attached with a such label or marker. The antibodies may also be used in affinity chromatography for isolating or purifying the BRCA2 protein, polypeptides or their functional equivalents.

EXAMPLE 1

Determination of the Coding Sequence Haplotypes of the BRCA2 Gene From Normal Individuals

Approximately 150 volunteers were screened in order to identify individuals with no cancer history in their immediate family (i.e. first and second degree relatives). Each person was asked to fill out a hereditary cancer prescreening questionnaire (See TABLE I). Five of these were randomly chosen for end-to-end sequencing of their BRCA2 gene. A first degree relative is a parent, sibling, or

offspring. A second degree relative is an aunt, uncle, grandparent, grandchild, niece, nephew, or half-sibling.

Genomic DNA was isolated from white blood cells of five normal subjects selected from analysis of their answers to the questions above. Dideoxy sequence analysis was performed following polymerase chain reaction amplification.

All exons of the BRCA2 gene were subjected to direct dideoxy sequence analysis by asymmetric amplification using the polymerase chain reaction (PCR) to generate a single stranded product amplified from this DNA sample. Shuldiner, *et al., Handbook of Techniques in Endocrine Research*, p. 457-486, DePablo, F., Scanes, C., eds., Academic Press, Inc., 1993. Fluorescent dye was attached for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer® cat# 401628). DNA sequencing was performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) automated sequencer (Model 377). The software used for analysis of the resulting data was "Sequence Navigator" purchased through ABI.

1. Polymerase Chain Reaction (PCR) Amplification

Genomic DNA (100 nanograms) extracted from white blood cells of five normal subjects. Each of the five samples was sequenced end to end. Each sample was amplified in a final volume of 25 microliters containing 1 microliter (100 nanograms) genomic DNA, 2.5 microliters 10X PCR buffer (100 mM Tris, pH 8.3, 500 mM KCl, 1.2 mM $MgCl_2$), 2.5 microliters 10X dNTP mix (2 mM each nucleotide), 2.5 microliters forward primer, 2.5 microliters reverse primer, and 1 microliter Taq polymerase (5 units), and 13 microliters of water.

The primers in TABLE II below were used to carry out amplification of the various sections of the BRCA2 gene samples. The primers were synthesized on an DNA/RNA Synthesizer Model 394®.

Thirty-five cycles were performed, each consisting of denaturing (95°C; 30 seconds), annealing (55°C; 1 minute), and extension (72°C; 90 seconds), except during the first cycle in which the denaturing time was increased to 5 minutes, and during the last cycle in which the extension time was increased to 5 minutes.

PCR products were purified using Qia-quick® PCR purification kits (Qiagen®, cat# 28104; Chatsworth, CA). Yield and purity of the PCR product are determined spectrophotometrically at OD_{260} on a Beckman DU 650 spectrophotometer.

2. Dideoxy Sequence Analysis

Fluorescent dye was attached to PCR products for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer® cat # 401628). DNA sequencing was performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) Foster City, CA., automated sequencer (Model 377). The software used for analysis of the resulting data was "Sequence Navigator®" purchased through ABI.

3. RESULTS

Based upon the sequencing of the five normal individuals, it was determined that the standard sequence found in both GenBank and BIC were inaccurate. In Genbank, a 10 bp stretch (5'-TTTATTTTAG-3') was mistakenly listed as exonic at the 5' end of exon 5 while it should be intronic which would not be included in the cDNA and resultant protein. In addition, a more detrimental error that has the significant potential to lead to an incorrect diagnosis of breast cancer propensity exists in both Genbank and BIC: a sequence of 16 bp (5'-GTGTTCTCATAAACAG-3') should be at the end of exon 15, but instead is listed at the beginning of exon 16 in the database. The disclosure and listing of GenBank is shown in Figure 1. The correct intron/exon sequence of BRCA2 is presented in Figure 2, wherein,

(1) a 10 bp stretch (5'-TTTATTTTAG-3') is intronic at 3' end of intron 4, rather than at the 5' end of exon 5 (corrected exon 5 is listed as SEQ. ID. NO: 1) and

(2) a 16 bp stretch (5'-GTGTTCTCATAAACAG-3') is exonic at the 3' end of exon 15, rather than at the 5' end of exon 16 (corrected exons 15 and 16 are listed as SEQ. ID. No: 2 and 3 respectively)

The BIC BRCA2 sequence also contains sequence errors in which a strech of nine nucleotides at positions 5554-5460 is listed as CGTTTGTGT (amino acids: Arg-

Leu-Cys). The correct sequence at these positions is GTTTGTGTT (amino acids: Val-Cys-Val). In addition, the BIC BRCA2 nuclotides at positions 2024 (codon 599), 4553 (codon 1442), 4815 (codon 1529), 5841 (codon 1871), and 5972 (codon 1915) are T, T, A, C, and T respectively, wherein the correct nucleotides at these positions are C, C, G, T, and C respectively. Among them, the nuclotide errors at codon 599, 1442, 1915 result in amino acids changes.

Additional differences in the nucleic acids of the five normal individuals were found in ten polymorphic locations. The changes and their positions are found in TABLE III. The individual haplotypes of each chromosome of BRCA2 are displayed in FIGURE 3. In each case, the initial haplotype reported in Genbank (accession number U43746) was subtracted to determine the new haplotypes OMI 1-5. Thus, the Genbank sequence only represents 50% of the haplotypes found; the five new BRCA2 $^{(omi\ 1\text{-}5)}$ DNA sequences are shown as SEQ. ID. NO: 4, 6, 8, 10, and 12, respectively (See FIGURE 3), and the corresponding polypeptides are listed as SEQ. ID. NO: 5, 7, 9, 11, and 13 respectively. In combination, these seven haplotypes represent a functional allele profile for the BRCA2 gene.

The data show that for each of the samples, all exons of BRCA2 were identical except in the region of ten polymorphisms. Six of these polymorphisms were previously identified (Tartigan *et al.*, *Nature Genetics* 12: 333-337 (1996); Phelan *et al.*, *Nature Genetics* 13: 120-122 (1996); Couch *et al.*, *Nature Genetics* 13: 123-125 (1996); Teng, *et al.*, *Nature Genetics* 13: 241-244 (1996); Schubert *et al* 60: 1031-1040 (1997)), but four were unique to this work. Even though the individual polymorphisms may have been identified, none of these complete haplotypes has been previously determined.

TABLE I

Hereditary Cancer Pre-Screening Questionnaire

Part A: Answer the following questions about your family

1. To your knowledge, has anyone in your family been diagnosed with a very specific hereditary colon disease called Familial Adenomatous Polyposis (FAP)?

2. To your knowledge, have you or any aunt had breast cancer diagnosed before the age 35?

3. Have you had Inflammatory Bowel Disease, also called Crohn's Disease or Ulcerative Colitis, for more than 7 years?

Part B: Refer to the list of cancers below for your responses **only** to questions in Part B

Bladder Cancer	Lung Cancer	Pancreatic Cancer
Breast Cancer	Gastric Cancer	Prostate Cancer
Colon Cancer	Malignant Melanoma	Renal Cancer
Endometrial Cancer	Ovarian Cancer	Thyroid Cancer

4. Have your mother or father, your sisters or brothers or your children had any of the listed cancers?

5 Have there been diagnosed in your mother's brothers or sisters, or your mother's parents more than one of the cancers in the above list?

6. Have there been diagnosed in your father's brothers or sisters, or your father's parents more than one of the cancers in the above list?

Part C: Refer to the list of relatives below for responses **only** to questions in Part C

You	Your mother
Your sisters or brothers	Your mother's sisters or brothers (maternal aunts & uncles)
Your children	Your mother's parents (maternal grandparents)

7. Have there been diagnosed in these relatives 2 or more identical types of cancer? Do not count "simple" skin cancer, also called basal cell or squamous cell skin cancer.

8. Is there a total of 4 or more of any cancers in the list of relatives above other than "simple" skin cancers?

Part D: Refer to the list of relatives below for responses **only** to questions in Part D.

You	Your father
Your sisters or brothers	Your father's sisters or brothers (paternal aunts and uncles)
Your children	Your father's parents (paternal grandparents)

9. Have there been diagnosed in these relatives 2 or more identical types of cancer? Do not count "simple" skin cancer, also called basal cell or squamous cell skin cancer.

10. Is there a total of 4 or more of any cancers in the list of relatives above other than "simple" skin cancers?

TABLE II
BRCA2 PRIMER SEQUENCES

Exon	Label	SEQUENCE (5' TO 3') NOTE: M13 TAIL INCLUDED M13 FORWARD = TGT AAA ACG ACG GCC AGT M13 REVERSE = CAG GAA ACA GCT ATG ACC	Oligo Length	PCR Product Length	SEQ. ID. Number
2	BRCA2-2F	5'-TGA GTT TTA CCT CAG TCA CA-3'	20	263	14
2	BRCA2-2R/M 13R	5'-CAG GAA ACA GCT ATG ACC CTG TGA CGT ACT GGG TTT TTA GC-3'	41		15
3	BRCA2-3FII	5'-GAT CTT TAA CTG TTC TGG GTC ACA-3'	24	364	16
3	BRCA2-3RII	5'-CCC AGC ATG ACA CAA TTA ATG A-3'	22		17
4	BRCA2-4F/M 13F	5'-TGT AAA ACG ACG GCC AGT AGA ATG CAA ATT TAT AAT CCA GAG TA-3'	44	268	18
4	BRCA2-4R-1A	5'-ATC AGA TTC ATC TTT ATA GAA C-3'	22		19
5&6	BRCA2-5+6F/M13F	5'-TGT AAA ACG ACG GCC AGT TGT GTT GGC ATT TTA AAC ATC A-3'	40	453	20
5&6	BRCA2-5+6R/M13R	5'-CAG GAA ACA GCT ATG ACC CAG GGC AAA GGT ATA ACG CT-3'	38		21
7	BRCA2-7F/M13F	5'-TGT AAA ACG ACG GCC AGT TAA GTG AAA TAA AGA GTG AA-3'	38	248	22
7	BRCA2-7R/M13R	5'-CAG GAA ACA GCT ATG ACC AGA AGT ATT AGA GAT GAC-3'	36		23
8	BRCA2-8F/M13F	5'-TGT AAA ACG ACG GCC AGT GCC ATA TCT TAC CAC CTT GTG A-3'	40	319	24
	BRCA2-8FIA	5'-TTG CAT TCT AGT GAT AAT ATA C-3'	22	143	25
8	BRCA2-8RIA	5'-AAT TGT TAG CAA TTT CAA C-3'	19		26
9	BRCA2-9F/M13F	5'-TGT AAA ACG ACG GCC AGT TGG ACC TAG GTT GAT TGC AGA T-3'	40	338	27
9	BRCA2-9R/M13R	5'-CAG GAA ACA GCT ATG ACC TAA ACT GAG ATC ACG GGT GAC A-3'	40		28
10A	BRCA2-10AF	5'-GAA TAA TAT AAA TTA TAT GGC TTA-3'	24	255	29
10A	BRCA2-10AR/M13R	5'-CAG GAA ACA GCT ATG ACC CCT AGT CTT GCT AGT TCT T-3'	37		30
10B	BRCA2-10BF/M13F	5'- TGT AAA ACG ACG GCC AGT ARC TGA AGT GGA ACC AAA TGA TAC-3'	42	621	31
10B	BRCA2-10BR/M13R	5'- CAG GAA ACA GCT ATG ACC ACG TGG CAA AGA ATT CTC TGA AGT AA-3'	44		32

TABLE II
BRCA2 PRIMER SEQUENCES

Exon	Label	SEQUENCE (5' TO 3') NOTE: M13 TAIL INCLUDED M13 FORWARD = TGT AAA ACG ACG GCC AGT M13 REVERSE = CAG GAA ACA GCT ATG ACC	Oligo Length	PCR Product Length	SEQ. ID. Number
10C	BRCA2-10CF/M13F	5'-TGT AAA ACG ACG GCC AGT CAG CAT CTT GAA TCT CAT ACA G-3'	40	508	33
10C	BRCA2-10CRII	5'-AGA CAG AGG TAC CTG AAT C-3'	19		34
11	BRCA2-11AF-M13	5'- TGT AAA ACG ACG GCC AGT TGG TAC TTT AAT TTT GTC ACT T-3'	40	304	35
11	BRCA2-11AR-M13	5'-CAG GAA ACA GCT ATG ACC TGC AGG CAT GAC AGA GAA T-3'	37		36
11	BRCA2-11BF	5'-AAG AAG CAA AAT GTA ATA AGG A-3'	22	411	37
11	BRCA2-11BR	5'-CAT TTA AAG CAC ATA CAT CTT G-3'	22		38
11	BRCA2-11CF	5'-TCT AGA GGC AAA GAA TCA TAC-3'	21	349	39
11	BRCA2-11CR	5'-CAA GAT TAT TCC TTT CAT TAG C-3'	22		40
11	BRCA2-11DF	5'-AAC CAA AAC ACA AAT CTA AGA G-3'	22	344	41
11	BRCA2-11DR	5'-GTC ATT TTT ATA TGC TGC TTT AC-3'	23		42
11	BRCA2-11EF	5'-GGT TTT ATA TGG AGA CAC AGG-3'	21	369	43
11	BRCA2-11ER	5'-GTA TTT ACA ATT TCA ACA CAA GC-3'	23		44
11	BRCA2-11FF	5'-ATC ACA GTT TTG GAG GTA GC-3'	20	368	45
11	BRCA2-11FR	5'-CTG ACT TCC TGA TTC TTC TAA-3'	21		46
11	BRCA2-11GF	5'-CTC AGA TGT TAT TTT CCA AGC-3'	21	366	47
11	BRCA2-11GR	5'-CTG TTA AAT AAC CAG AAG CAC-3'	21		48
11	BRCA2-11HF	5'-AGG TAG ACA GCA GCA AGC-3'	18	360	49
11	BRCA2-11HR	5'-GTA ATA TCA GTT GGC ATT TAT T-3'	22		50
11	BRCA2-11IF	5'-TGC AGA GGT ACA TCC AAT AAG-3'	21	326	51
11	BRCA2-11IR	5'-GAT CAG TAA ATA GCA AGT CCG-3'	21		52
11	BRCA2-11JF	5'-TAC TGA AAA TGA AGA TAA CAA AT-3'	23	477	53

TABLE II
BRCA2 PRIMER SEQUENCES

Exon	Label	SEQUENCE (5' TO 3') NOTE: M13 TAIL INCLUDED M13 FORWARD = TGT AAA ACG ACG GCC AGT M13 REVERSE = CAG GAA ACA GCT ATG ACC	Oligo Length	PCR Product Length	SEQ. ID. Number
11	BRCA2-11JR	5'-ATT TTG TTC TTT CTT ATG TCA G-3'	22		54
11	BRCA2-11KF-M13	5'-TGT AAA ACG ACG GCC AGT CTA CTA AAA CGG AGC AA-3'	35	382	55
11	BRCA2-11KR-M13	5'-CAG GAA ACA GCT ATG ACC GTA TGA AAA CCC AAC AG-3'	35		56
11	BRCA2-11LF	5'-CAC AAA ATA CTG AAA GAA AGT G-3'	22	374	57
11	BRCA2-11LR	5'-GGC ACC ACA GTC TCA ATA G-3'	19		58
11	BRCA2-11MF	5'-GCA AAG ACC CTA AAG TAC AG-3'	20	409	59
11	BRCA2-11MR	5'-CAT CAA ATA TTC CTT CTC TAA G-3'	22		60
11	BRCA2-11NF-M13	5'-TGT AAA ACG ACG GCC AGT GAA AAT TCA GCC TTA GC-3'	35	306	61
11	BRCA2-11NR-M13	5'- CAG GAA ACA GCT ATG ACC ATC AGA ATG GTA GGA AT-3'	35		62
11	BRCA2-11OF	5'-GTA CTA TAG CTG AAA ATG ACA A-3'	22	383	63
11	BRCA2-11OR	5'-ACC ACT GGC TAT CCT AAA TG-3'	20		64
11	BRCA2-11PF	5'-TGA AGA TAT TTG CGT TGA GG-3'	20	355	65
11	BRCA2-11PR	5'-GTC AGC AAA AAC CTT ATG TG-3'	20		66
11	BRCA2-11QF	5'-ACG AAA ATT ATG GCA GGT TGT-3'	21	337	67
11	BRCA2-11QR	5'-CTT GTC TTG CGT TTT GTA ATG-3'	21		68
11	BRCA2-11RF	5'-GCT TCA TAA GTC AGT CTC AT-3'	20	360	69
11	BRCA2-11RR	5'-TCA AAT TCC TCT AAC ACT CC-3'	20		70
11	BRCA2-11SF-M13	5'-TGT AAA ACG ACG GCC AGT TAC AGC AAG TGG AAA GC-3'	35	458	71
11	BRCA2-11SR-M13	5'-CAG GAA ACA GCT ATG ACC AAG TTT CAG TTT TAC CAA T-3'	37		72
11	BRCA2-11TF	5'-GTT CTT CAG AAA ATA ATC ACT C-3'	22	344	73
11	BRCA2-11TR	5'-TGT AAA AAG AGA ATG TGT GGC-3'	21		74

TABLE II
BRCA2 PRIMER SEQUENCES

Exon	Label	SEQUENCE (5' TO 3') NOTE: M13 TAIL INCLUDED M13 FORWARD = TGT AAA ACG ACG GCC AGT M13 REVERSE = CAG GAA ACA GCT ATG ACC	Oligo Length	PCR Product Length	SEQ. ID. Number
11	BRCA2-11UF-M13	5'-TGT AAA ACG ACG GCC AGT ACT TTT TCT GAT GTT CCT GTG-3'	39	328	75
11	BRCA2-11UR-M13	5'-CAG GAA ACA GCT ATG ACC TAA AAA TAG TGA TTG GCA ACA-3'	39		76
12	BRCA2-12F/M13F	5'-TGT AAA ACG ACG GCC AGT AGT GGT GTT TTA AAG TGG TCA AAA-3'	42	391	77
12	BRCA2-12R/M13R	5'-CAG GAA ACA GCT ATG ACC GGA TCC ACC TGA GGT CAG AAT A-3'	40		78
13	BRCA2/13-2F	5'-TAA CAT TTA AGC ATC CGT TAC-3'	21	310	79
13	BRCA2/13-2R	5'-AAA CGA GAC TTT TCT CAT ACT GTA TTA G-3'	28		80
14	BRCA2-14F	5'-ACC ATG TAG CAA ATG AGG GTC T-3'	22	391	81
14	BRCA2-14AR	5'-GCT TTT GTC TGT TTT CCT CCA A-3'	22		82
15	BRCA2-15-2F	5'-CCA GGG GTT GTG CTT TTT AAA-3'	21	284	83
15	BRCA2-15FUT/M13-R	5'-CAG GAA ACA GCT ATG ACC ACT CTG TCA TAA AAG CCA TC-3'	38		84
16	BRCA2-16AF	5'-TTT GGT TTG TTA TAA TTG TTT TTA-3'	24	394	85
16	BRCA2-16AR	5'-CCA ACT TTT TAG TTC GAG AG-3'	20		86
17	BRCA2-17F	5'-TTC AGT ATC ATC CTA TGT G-3'	19	282	87
17	BRCA2-17AR	5'-AGA AAC CTT AAC CCA TAC TG-3'	20		88
18	BRCA2-18FUT/M13-AF	5'-TGT AAA ACG ACG GCC AGT GAA TTC TAG AGT CAC ACT TCC-3'	39	275	89
18	BRCA2-18R/M13R	5'-CAG GAA ACA GCT ATG ACC TTT AAC TGA ATC AAT GAC TG-3'	38		90
19	BRCA2-19F/M13F	5'-TGT AAA ACG ACG GCC AGT AAG TGA ATA TTT TTA AGG CAG TT-3'	41	355	91
19	BRCA2-19FUT/M13-R	5'-CAG GAA ACA GCT ATG ACC AAG AGA CCG AAA CTC CAT CTC-3'	39		92
20	BRCA2-20F/M13F	5'-TGT AAA ACG ACG GCC AGT CAC TGT GCC TGG CCT GAT AC-3'	38	296	93
20	BRCA2-20R/M13R	5'-CAG GAA ACA GCT ATG ACC ATG TTA AAT TCA AAG TCT CTA-3'	39		94
21	BRCA2-21F/M13F	5'-TGT AAA ACG ACG GCC AGT GGG TGT TTT ATG CTT GGT TCT-3'	39	304	95

TABLE II
BRCA2 PRIMER SEQUENCES

Exon	Label	SEQUENCE (5' TO 3') NOTE: M13 TAIL INCLUDED M13 FORWARD = TGT AAA ACG ACG GCC AGT M13 REVERSE = CAG GAA ACA GCT ATG ACC	Oligo Length	PCR Product Length	SEQ. ID. Number
21	BRCA2-21R/M13R	5'-CAG GAA ACA GCT ATG ACC CAT TTC AAC ATA TTC CTT CCT G-3'	40		96
22	BRCA2-22F-1A	5'-AAC CAC ACC CTT AAG ATG A-3'	19	453	97
22	BRCA2-22R-1A	5'-GCA TTA GTA GTG GAT TTT GC-3'	20		98
23	BRCA2-23FII	5'-TCA CTT CCA TTG CAT C-3'	16	290	99
23	BRCA2-23RII	5'-TGC CAA CTG GTA GCT CC-3'	17		100
24	BRCA2-24 2F	5'-TAC AGT TAG CAG CGA CAA AA-3'	20	373	101
24	BRCA2-24R/M13R	5'-CAG GAA ACA GCT ATG ACC ATT TGC CAA CTG GTA GCT CC-3'	38		102
25	BRCA2-25F-7/23	5'-GCT TTC GCC AAA TTC AGC TA-3'	20	427	103
25	BRCA2-25R-7/23	5'-TAC CAA AAT GTG TGG TGA TG-3'	20		104
26	BRCA2/26-2F	5'-AAT CAC TGA TAC TGG TTT TG-3'	20	530	105
26	BRCA2/26-2R	5'-TAT ACT TAC AGG AGC CAC AT-3'	20		106
27A	BRCA2-27AF-1A	5'-CTG TGT GTA ATA TTT GCG-3'	18	495	107
27A	BRCA2-27AR/M13R	5'-CAG GAA ACA GCT ATG ACG GCA AGT TCT TCG TCA GCT ATT G-3'	40		108
27B	BRCA2-27BF/M13F	5'-TGT AAA ACG ACG GCC AGT GAA TTC TCC TCA GAT GAC TCC A-3'	40	417	109
27B	BRCA2-27BR/M13R	5'-CAG GAA ACA GCT ATG ACC TCT TTG CTC ATT GTG CAA CA-3'	38		110

TABLE III
NORMAL PANEL TYPING

Position nt/codon	Nucleotide Change	Amino Acid Change	1	2	3	4	5	Frequency
1093/289	AAT → CAT	Asn → His	A/A	A/C	A/A	A/A	A/C	A = .8 C = .2
1342/372	AAT → CAT	Asn → His	A/C	A/A	A/C	A/C	A/C	A = 0.6 C = 0.4
1593/455	TCA → TCG	Ser → Ser	A/A	A/A	A/A	A/A	A/G	A = 0.9 G = 0.1
2457/743	CAT → CAC	His → His	T/T	C/T	T/T	T/T	C/T	T = 0.8 C = 0.2
2908/894	GTA → ATA	Val → Ile	G/G	G/G	G/G	G/G	A/G	G = 0.9 A = 0.1
3199/991	AAC → GAC	Asn → Asp	A/A	A/G	A/A	A/A	A/G	A = 0.8 G = 0.2

TABLE III
NORMAL PANEL TYPING

Position nt/codon	Nucleotide Change	Amino Acid Change	1	2	3	4	5	Frequency
3624/1132	AAA → AAG	Lys → Lys	A/A	A/G	A/A	A/G	A/A	A = 0.8 G = 0.2
4035/1269	GTT → GTC	Val → Val	C/T	T/T	T/T	T/T	T/T	T = 0.9 C = 0.1
7470/2414	TCA → TCG	Ser → Ser	A/A	A/G	A/A	A/G	A/A	A = 0.8 G = 0.2
9079/2951	GCC → ACC	Ala → Thr	G/G	G/G	G/G	G/G	A/G	G = 0.9 A = 0.1

EXAMPLE 2

Determination Of A Normal Individual Using BRCA2$^{(OMI\ 1\text{-}5)}$ and The Ten Polymorphisms For Reference

A person skilled in the art of genetic susceptibility testing will find the present invention useful for:

a) identifying individuals having a normal BRCA2 gene;

b) avoiding misinterpretation of normal polymorphisms found in the normal population.

Sequencing was carried out as in EXAMPLE 1 using a blood sample from the patient in question. However, the BRCA2$^{(omi1\text{-}5)}$ sequences were used for reference and any polymorphic sites seen in the patient were compared to the nucleic acid sequences listed above for normal codons at each polymorphic site. A normal sample is one which is comparable to the BRCA2$^{(omi\ 1\text{-}5)}$ sequences and contains only minor variations which occur at minor polymorphic sites. The allelic variations which occur at each of the polymorphic sites are paired here for reference.

- AAT (Asn) and CAT (His) at position 1093 (codon 289)
- CAT (His) and AAT (Asn) at position 1342 (codon 372)
- TCA (Ser) and TCG (Ser) at position 1593 (codon 455)
- CAT (His) and CAC (His) at position 2457 (codon 743)
- GTA (Val) and ATA (Ile) at position 2908 (codon 894)
- AAC (Asn) and GAC (Asp) at position 3199 (codon 991)
- AAA (Lys) and AAG (Lys) at position 3624 (codon 1132)
- GTT (Val) and GTC (Val) at position 4035 (codon 1269)
- TCA (Ser) and TCG (Ser) at position 7470 (codon 2414)
- GCC (Ala) and ACC (Thr) at position 9079 (codon 2951)

The availability of these polymorphic pairs provides added assurance that one skilled in the art can correctly interpret the polymorphic variations without mistaking a normal variation for a mutation.

All exons of the BRCA2 gene are subjected to direct dideoxy sequence analysis by asymmetric amplification using the polymerase chain reaction (PCR) to generate a single stranded product amplified from this DNA sample. Shuldiner, *et*

al., Handbook of Techniques in Endocrine Research, p. 457-486, DePablo, F., Scanes, C., eds., Academic Press, Inc., 1993. Fluorescent dye is attached for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer® cat# 401628). DNA sequencing is performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) automated sequencer (Model 377). The software used for analysis of the resulting data is "Sequence Navigator" purchased through ABI.

1. Polymerase Chain Reaction (PCR) Amplification

The PCR primers used to amplify a patient's sample BRCA2 gene are listed in TABLE II. The primers were synthesized on a DNA/RNA Synthesizer Model 394®. Thirty-five cycles are of amplification are performed, each consisting of denaturing (95°C; 30 seconds), annealing (55°C; 1 minute), and extension (72°C; 90 seconds), except during the first cycle in which the denaturing time is increased to 5 minutes and during the last cycle in which the extension time is increased to 5 minutes.

PCR products are purified using Qia-quick® PCR purification kits (Qiagen®, cat# 28104; Chatsworth, CA). Yield and purity of the PCR product are determined spectrophotometrically at OD_{260} on a Beckman DU 650 spectrophotometer.

2. Dideoxy Sequence Analysis

Fluorescent dye is attached to PCR products for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer® cat# 401628). DNA sequencing is performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) Foster City, CA., automated sequencer (Model 377). The software used for analysis of the resulting data is "Sequence Navigator®" purchased through ABI. The BRCA2$^{(omi\ 1\text{-}5)}$ sequences were entered sequentially into the Sequence Navigator software as the standards for comparison. The Sequence Navigator software compares the patient sample sequence to each BRCA2 $^{(omi\ 1\text{-}5)}$ standard, base by base. The Sequence Navigator highlights all differences between the standards (omi 1-5) and the patient's sample sequence.

A first technologist checks the computerized results by comparing visually the BRCA2 (omi 1-5) standards against the patient's sample, and again highlights any differences between the standard and the sample. The first primary technologist then interprets the sequence variations at each position along the sequence. Chromatograms from each sequence variation are generated by the Sequence Navigator and printed on a color printer. The peaks are interpreted by the first primary technologist and a second primary technologist. A secondary technologist then reviews the chromatograms. The results are finally interpreted by a geneticist. In each instance, a variation is compared to known normal polymorphisms for position and base change.

3. Results

The patient's BRCA2 sequence was found to be heterozygous at seven nucleotide positions: 1093 (A/C), 1342 (A/C), 1593 (A/G), 2457 (C/T), 2908 (A/G), 3199 (A/G) and 9079 (A/G). In addition, this changes five amino acids in the polypeptide product: Asn to His at codon 289, Asn to His at codon 372, Val to Ile at codon 894, Asn to Asp at codon 991, and Ala to Thr at codon 2951. The question arises whether any or all of these changes have significance to the patient. Comparison of the patient's results to the BRCA (omi 1-5) haplotypes demonstrates that it matches one of the BRCA2 omi standards (#5), and thus the patient sample is interpreted as carrying a normal gene sequence without causing any elevation in their risk status for breast cancer.

EXAMPLE 3

DETERMINING THE PRESENCE OF A MUTATION IN EXON 11 OF THE BRCA2 GENE USING BRCA2(omi1-5)

A person skilled in the art of genetic susceptibility testing will find the present invention useful for determining the presence of a known or previously unknown mutation in the BRCA2 gene. A list of mutations of BRCA2 is publicly available in the Breast Cancer Information Core at http://www.nchgr.nih.gov/dir/lab_transfer/bic. This data site became publicly available on November 1, 1995. Friend, S. *et al.* *Nature Genetics* 11:238, (1995).

In this example, a mutation in exon 11 is characterized by amplifying the region of the mutation with a primer set which amplifies the region of the mutation. Sequencing was carried out as in Example 1 using a blood sample from the patient in question. Specifically, exon 11 of the BRCA2 gene is subjected to direct dideoxy sequence analysis by asymmetric amplification using the polymerase chain reaction (PCR) to generate a single stranded product amplified from this DNA sample. Shuldiner, *et al., Handbook of Techniques in Endocrine Research*, p. 457-486, DePablo, F., Scanes, C., eds., Academic Press, Inc., 1993. Fluorescent dye is attached for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer® cat# 401628). DNA sequencing is performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) automated sequencer (Model 377). The software used for analysis of the resulting data is "Sequence Navigator" purchased through ABI.

1. Polymerase Chain Reaction (PCR) Amplification

Genomic DNA (100 nanograms) extracted from white blood cells of the subject is amplified in a final volume of 25 microliters containing 1 microliter (100 nanograms) genomic DNA, 2.5 microliters 10X PCR buffer (100 mM Tris, pH 8.3, 500 mM KCl, 1.2 mM $MgCl_2$), 2.5 microliters 10X dNTP mix (2 mM each nucleotide), 2.5 microliters forward primer (BRCA2-11Q-F, 10 micromolar solution), 2.5 microliters reverse primer (BRCA2-11Q-R, 10 micromolar solution),and 1 microliter Taq polymerase (5 units), and 13 microliters of water.

The PCR primers used to amplify segment Q of exon 11 (where the mutation 6174delT is found) are as follows:

BRCA2-11Q-F: 5'- ACG' AAA' ATT' ATG' GCA' GGT' TGT-3'

BRCA2-11Q-R: 5'- CTT' GTC' TTG' CGT' TTT' GTA' ATG-3'

The primers are synthesized on an DNA/RNA Synthesizer Model 394®. Thirty-five cycles are performed, each consisting of denaturing (95°C; 30 seconds), annealing (55°C; 1 minute), and extension (72°C; 90 seconds), except during the

first cycle in which the denaturing time is increased to 5 minutes, and during the last cycle in which the extension time is increased to 5 minutes.

PCR products are purified using Qia-quick® PCR purification kits (Qiagen®, cat# 28104; Chatsworth, CA). Yield and purity of the PCR product are determined spectrophotometrically at OD_{260} on a Beckman DU 650 spectrophotometer.

2. Dideoxy Sequence Analysis

Fluorescent dye is attached to PCR products for automated sequencing using the Taq Dye Terminator Kit (Perkin-Elmer® cat# 401628). DNA sequencing is performed in both forward and reverse directions on an Applied Biosystems, Inc. (ABI) Foster City, CA., automated sequencer (Model 377). The software used for analysis of the resulting data is "Sequence Navigator®" purchased through ABI. The BRCA2$^{(omi\ 1\text{-}5)}$ sequence is entered into the Sequence Navigator software as the Standard for comparison. The Sequence Navigator software compares the sample sequence to the BRCA2$^{(omi)}$ standard, base by base. The Sequence Navigator highlights all differences between the BRCA2$^{(omi)}$ normal DNA sequence and the patient's sample sequence.

A first technologist checks the computerized results by comparing visually the BRCA2$^{(omi\ 1\text{-}5)}$ standard against the patient's sample, and again highlights any differences between the standard and the sample. The first primary technologist then interprets the sequence variations at each position along the sequence. Chromatograms from each sequence variation are generated by the Sequence Navigator and printed on a color printer. The peaks are interpreted by the first primary technologist and a second primary technologist. A secondary technologist then reviews the chromatograms. The results are finally interpreted by a geneticist. In each instance, a sequence variation is compared to known normal polymorphisms for position and base change. The ten frequent polymorphisms which occur in BRCA2 are:

- AAT (Asn) and CAT (His) at position 1093 (codon 289)
- CAT (His) and AAT (Asn) at position 1342 (codon 372)
- TCA (Ser) and TCG (Ser) at position 1593 (codon 455)

- CAT (His) and CAC (His) at position 2457 (codon 743)
- GTA (Val) and ATA (Ile) at position 2908 (codon 894)
- AAC (Asn) and GAC (Asp) at position 3199 (codon 991)
- AAA (Lys) and AAG (Lys) at position 3624 (codon 1132)
- GTT (Val) and GTC (Val) at position 4035 (codon 1269)
- TCA (Ser) and TCG (Ser) at position 7470 (codon 2414)
- GCC (Ala) and ACC (Thr) at position 9079 (codon 2951)

3. Results

Using the above PCR amplification and standard fluorescent sequencing technology, the 6174delT mutation may be found. Mutations are noted by the length of non-matching sequence variation. Such a lengthy mismatch pattern occurs with deletions and insertions. This mutation is named in accordance with the suggested nomenclature for naming mutations, Beaudet, A *et al., Human Mutation* 2:245-248, (1993). The 6174delT mutation at codon 1982 of the BRCA2 gene lies in segment "Q" of exon 11. The DNA sequence results demonstrate the presence of a one base pair deletion of a T at nucleotide 6174 of the BRCA2$^{(omi\ 1\text{-}5)}$ sequences. This mutation interrupts the normal reading frame of the BRCA2 transcript, resulting in the appearance of an in-frame terminator (TAG) at codon position 2003. This mutation is, therefore, predicted to result in a truncated, and most likely, non-functional protein.

EXAMPLE 4

GENERATION OF MONOCLONAL AND POLYCLONAL ANTIBODIES USING GST-BRCA2 FUSION PROTEIN AS AN IMMUNOGEN

DNA primers are used to amplify a fragment of BRCA2 using PCR technology. The product is then digested with suitable restriction enzymes and fused in frame with the gene encoding glutathione S-transferase (GST) in *Escherichia coli* using GST expression vector pGEX (Pharmacia Biotech Inc.) The expression of the fusion protein is induced by the addition of isopropyl-β-thiogalactopyranoside. The bacteria are then lysed and the overexpressed fusion protein is purified with glutathione-sepharose beads. The fusion protein is then verified by SDS/PAGE gel and N-terminus protein sequencing. The purified protein

is used to immunize rabbits according to standard procedures described in Harlow & Lane (1988). Polycolonal antibody is collected from the serum several weeks after and purified using known methods in the art. Monoclonal antibodies against all or fragments of BRCA2 protein, polypeptides, or functional equivalents are obtained using hybridoma technology, see also Harlow & Lane (1988). The BRCA2 protein or polypeptide is coupled to the carrier keyhole limpet hemocyanin in the presence of glutaraldehyde. The conjugated immunogen is mixed with an adjuvant and injected into rabbits. Spleens from antibody-containing rabbits are removed. The B-cells isolated from spleen are fused to myeloma cells using polyethylene glycol (PEG) to promote fusion. The hybrids between the myeloma and B-cells are selected and screened for the production of antibodies to immunogen BRCA2 protein or polypeptide. Positive cells are recloned to generate monoclonal antibodies.

EXAMPLE 5

DETECTION OF BRCA2 EXPRESSION IN HUMAN TISSUES AND CELL LINES

The expression of BRCA2 in human tissues is determined using Northern blot analysis. Human tissues include those from pancreas, testis, prostate, ovary, breast, small intestine, and colon are obtained from Clontech Laboratories, Inc., Palo Alto, CA. The poly(A)+ mRNA Northern blots from different human tissues is hybridized to BRCA2 cDNA probes according to manufacture protocol. The expression level is further conformed by RT-PCR using oligo-d(T) as a primer and other suitable primers.

For Northern Blot analysis of cancer cell lines, the human ovarian cancer cell line SKOV-3 and the human breast cancer cell line MCF-7 are obtained from the American Type Culture Collection. Total RNA is prepared by lysing cell in the presence of guanidinium isocyanate. Poly(A)$^+$ mRNA is isolated using the PolyATract mRNA isolation system from Promega, Madison, WI. The isolated RNA is then electrophoresed under denaturing conditions and transferred to Nylon membrane. The probe used for Northern blot is a fragment of BRCA2 sequence obtained by PCR amplification. The probes are labeled with [α-^{32}P] dCTP using a random-primed labeling kit (Amersham Life Science, Arlington Heights, IL).

EXAMPLE 6

EXPRESSION OF THE BRCA2 PROTEIN

The whole-cell extracts of BRCA2 transfected cells are subjected to immunoprecipitation and immunoblotting to determine the BRCA2 protein level. The BRCA2 protein or polypeptide is immunoprecipitated using anti-BRCA2 antibodies prepared according to Example 4. Samples are then fractionated using SDS/PAGE gel and transferred to nitrocellulose. Western blot of the BRCA2 protein or polypeptide is performed with the indicated antibodies. Antibody reaction is revealed using enhanced chemiluminescence reagents (Dupont New England Nuclear, Boston, MA).

EXAMPLE 7

USE OF THE BRCA2$^{(omi1-5)}$ GENE THERAPY

The growth of ovarian or breast cancer may be arrested by increasing the expression of the BRCA2 gene where inadequate expression of that gene is responsible for hereditary ovarian or breast cancer. Gene therapy may be performed on a patient to reduce the size of a tumor. The LXSN vector may be transformed with a BRCA2$^{(omi1-5)}$ coding sequence as presented SEQ ID NO:4, 6, 8, 10, or 12 or a fragment thereof.

Vector

The LXSN vector is transformed with a fragment of the wildtype BRCA2$^{(omi1-5)}$ coding sequence as set forth in SEQ ID NO:4, 6, 8, 10, or 12. The LXSN-BRCA2$^{(omi1-5)}$ retroviral expression vector is constructed by cloning a *Sal* I linkered BRCA2$^{(omi1-5)}$ cDNA or fragments thereof into the *Xho* I site of the vector LXSN. Constructs are confirmed by DNA sequencing. See Holt et al., *Nature Genetics* 12: 298-302 (1996). Retroviral vectors are manufactured from viral producer cells using serum free and phenol-red free conditions and tested for sterility, absence of specific pathogens, and absence of replication-competent retrovirus by standard assays. Retrovirus is stored frozen in aliquots which have been tested.

Patients receive a complete physical exam, blood, and urine tests to determine overall health. They may also have a chest X-ray, electrocardiogram, and appropriate radiologic procedures to assess tumor stage.

Patients with metastatic ovarian cancer are treated with retroviral gene therapy by infusion of recombinant LXSN-BRCA2$^{(omi1-5)}$ retroviral vectors into peritoneal sites containing tumor, between 10^9 and 10^{10} viral particles per dose. Blood samples are drawn each day and tested for the presence of retroviral vector by sensitive polymerase chain reaction (PCR)-based assays. The fluid which is removed is analyzed to determine:

1. The percentage of cancer cells which are taking up the recombinant LXSN-BRCA2$^{(omi1-5)}$ retroviral vector combination. Successful transfer of BRCA1 gene into cancer cells has been shown by both RT-PCR analysis and *in situ* hybridization. RT-PCR is performed with by the method of Thompson et al., *Nature Genetics* 9: 444-450 (1995), using primers derived from a BRCA2$^{(omi1-5)}$ coding sequence as in SEQ ID NO:4, 6, 8, 10, or 12 or fragments thereof. Cell lysates are prepared and immunoblotting is performed by the method of Jensen *et al., Nature Genetics* 12: 303-308 (1996) and Jensen *et al.*, *Biochemistry* 31: 10887-10892 (1992).

2. Presence of programmed cell death using APOTAG® *in situ* apoptosis detection kit (ONCOR, INC., Gaithersburg, Maryland) and DNA analysis.

3. Measurement of BRCA2 gene expression by slide immunofluorescence or Western blot.

Patients with measurable disease are also evaluated for a clinical response to LXSN-BRCA2$^{(omi1-5)}$ especially those that do not undergo a palliative intervention immediately after retroviral vector therapy. Fluid cytology, abdominal girth, CT scans of the abdomen, and local symptoms are followed.

For other sites of disease, conventional response criteria are used as follows:

1. Complete Response (CR), complete disappearance of all measurable lesions and of all signs and symptoms of disease for at least 4 weeks.

2. Partial Response (PR), decrease of at least 50% of the sum of the products of the 2 largest perpendicular diameters of all measurable lesions as determined by 2 observations not less than 4 weeks apart. To be considered a PR, no new lesions should have appeared during this period and none should have increased in size.

3. Stable Disease, less than 25% change in tumor volume from previous evaluations.

4. Progressive Disease, greater than 25% increase in tumor measurements from prior evaluations. The number of doses depends upon the response to treatment.

EXAMPLE 8

PROTEIN REPLACEMENT THERAPY

Therapeutically elevated level of functional BRCA2 protein may alleviate the absence or reduced endogenous BRCA2 tumor suppressing activity. Breast or ovarian cancer is treated by the administration of a therapeutically effective amount of the BRCA2 protein, a polypeptide, or its functional equivalent in a pharmaceutically acceptable carrier. Clinically effective delivery method is applied either locally at the site of the tumor or systemically to reach other metastasized locations with known protocols in the art. These protocols may employ the methods of direct injection into a tumor or diffusion using time release capsule. A therapeutically effective dosage is determined by one of skill in the art.

Breast or ovarian cancer may be prevented by the administration of a prophylactically effective amount of the BRCA2 protein, polypeptide, or its functional equivalent in a pharmaceutically acceptable carrier. Individuals with known risk for breast or ovarian cancer are subjected to protein replacement therapy to prevent tumorigenesis or to decrease the risk of cancer. Elevated risk for breast and ovarian cancer includes factors such as carriers of one or more known BRCA1 and BRCA2 mutations, late child bearing, early onset of menstrual period, late occurrence of menopause, and certain high risk dietary habits. Clinically effective delivery method is used with known protocols in the art, such as administration into peritoneal cavity, or using an implantable time release capsule. A prophylactically effective dosage is determined by one of skill in the art.

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Although the invention has been described with reference to the presently preferred embodiments, it should be understood that various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims.

SEQUENCE LISTING

(1) GENERAL INFORMATION

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(ii) TITLE OF THE INVENTION: NOVEL CODING SEQUENCE HAPLOTYPES OF THE HUMAN BRCA2 GENE

(iii) NUMBER OF SEQUENCES: 111

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(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Diskette
(B) COMPUTER: IBM Compatible
(C) OPERATING SYSTEM: DOS
(D) SOFTWARE: FastSEQ for Windows Version 2.0

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:

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(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 50 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: Genomic DNA
(ix) FEATURE:

(A) NAME/KEY: exon
(B) LOCATION: 1...50
(D) OTHER INFORMATION: Exon 5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

TCCTGTTGTT CTACAATGTA CACATGTAAC ACCACAAAGA GATAAGTCAG 50

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 182 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: Genomic DNA
(ix) FEATURE:

(A) NAME/KEY: exon
(B) LOCATION: 1...182
(D) OTHER INFORMATION: Exon 15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

ATTTAATTAC AAGTCTTCAG AATGCCAGAG ATATACAGGA TATGCGAATT AAGAAGAAAC 60
AAAGGCAACG CGTCTTTCCA CAGCCAGGCA GTCTGTATCT TGCAAAAACA TCCACTCTGC 120
CTCGAATCTC TCTGAAAGCA GCAGTAGGAG GCCAAGTTCC CTCTGCGTGT TCTCATAAAC 180
AG 182

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 188 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: Genomic DNA
(ix) FEATURE:

(A) NAME/KEY: exon
(B) LOCATION: 1...188
(D) OTHER INFORMATION: Exon 16

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

CTGTATACGT ATGGCGTTTC TAAACATTGC ATAAAAATTA ACAGCAAAAA TGCAGAGTCT 60
TTTCAGTTTC ACACTGAAGA TTATTTTGGT AAGGAAAGTT TATGGACTGG AAAAGGAATA 120
CAGTTGGCTG ATGGTGGATG GCTCATACCC TCCAATGATG GAAAGGCTGG AAAAGAAGAA 180
TTTTATAG 188

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10485 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 229...10482
(D) OTHER INFORMATION: BRCA2 (OMI1)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

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GGTGGCGCGA GCTTCTGAAA CTAGGCGGCA GAGGCGGAGC CGCTGTGGCA CTGCTGCGCC     60
TCTGCTGCGC CTCGGGTGTC TTTTGCGGCG GTGGGTCGCC GCCGGGAGAA GCGTGAGGGG    120
ACAGATTTGT GACCGGCGCG GTTTTTGTCA GCTTACTCCG GCCAAAAAAG AACTGCACCT    180
CTGGAGCGGA CTTATTTACC AAGCATTGGA GGAATATCGT AGGTAAAA ATG CCT ATT    237
                                                      Met Pro Ile
                                                       1

GGA TCC AAA GAG AGG CCA ACA TTT TTT GAA ATT TTT AAG ACA CGC TGC     285
Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys Thr Arg Cys
 5                  10                  15

AAC AAA GCA GAT TTA GGA CCA ATA AGT CTT AAT TGG TTT GAA GAA CTT     333
Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe Glu Glu Leu
20                  25                  30                  35

TCT TCA GAA GCT CCA CCC TAT AAT TCT GAA CCT GCA GAA GAA TCT GAA     381
Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu Glu Ser Glu
                40                  45                  50

CAT AAA AAC AAC AAT TAC GAA CCA AAC CTA TTT AAA ACT CCA CAA AGG     429
His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr Pro Gln Arg
            55                  60                  65

AAA CCA TCT TAT AAT CAG CTG GCT TCA ACT CCA ATA ATA TTC AAA GAG     477
Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile Phe Lys Glu
        70                  75                  80

CAA GGG CTG ACT CTG CCG CTG TAC CAA TCT CCT GTA AAA GAA TTA GAT     525
Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys Glu Leu Asp
    85                  90                  95

AAA TTC AAA TTA GAC TTA GGA AGG AAT GTT CCC AAT AGT AGA CAT AAA     573
Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser Arg His Lys
100                 105                 110                 115

AGT CTT CGC ACA GTG AAA ACT AAA ATG GAT CAA GCA GAT GAT GTT TCC     621
Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp Asp Val Ser
                120                 125                 130

TGT CCA CTT CTA AAT TCT TGT CTT AGT GAA AGT CCT GTT GTT CTA CAA     669
Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val Val Leu Gln
            135                 140                 145

TGT ACA CAT GTA ACA CCA CAA AGA GAT AAG TCA GTG GTA TGT GGG AGT     717
Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val Cys Gly Ser
        150                 155                 160
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TTG TTT CAT ACA CCA AAG TTT GTG AAG GGT CGT CAG ACA CCA AAA CAT      765
Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr Pro Lys His
    165                 170                 175

ATT TCT GAA AGT CTA GGA GCT GAG GTG GAT CCT GAT ATG TCT TGG TCA      813
Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met Ser Trp Ser
180                 185                 190                 195

AGT TCT TTA GCT ACA CCA CCC ACC CTT AGT TCT ACT GTG CTC ATA GTC      861
Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val Leu Ile Val
                200                 205                 210

AGA AAT GAA GAA GCA TCT GAA ACT GTA TTT CCT CAT GAT ACT ACT GCT      909
Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp Thr Thr Ala
            215                 220                 225

AAT GTG AAA AGC TAT TTT TCC AAT CAT GAT GAA AGT CTG AAG AAA AAT      957
Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu Lys Lys Asn
        230                 235                 240

GAT AGA TTT ATC GCT TCT GTG ACA GAC AGT GAA AAC ACA AAT CAA AGA     1005
Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr Asn Gln Arg
    245                 250                 255

GAA GCT GCA AGT CAT GGA TTT GGA AAA ACA TCA GGG AAT TCA TTT AAA     1053
Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn Ser Phe Lys
260                 265                 270                 275

GTA AAT AGC TGC AAA GAC CAC ATT GGA AAG TCA ATG CCA AAT GTC CTA     1101
Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro Asn Val Leu
                280                 285                 290

GAA GAT GAA GTA TAT GAA ACA GTT GTA GAT ACC TCT GAA GAA GAT AGT     1149
Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu Glu Asp Ser
            295                 300                 305

TTT TCA TTA TGT TTT TCT AAA TGT AGA ACA AAA AAT CTA CAA AAA GTA     1197
Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu Gln Lys Val
        310                 315                 320

AGA ACT AGC AAG ACT AGG AAA AAA ATT TTC CAT GAA GCA AAC GCT GAT     1245
Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala Asn Ala Asp
    325                 330                 335

GAA TGT GAA AAA TCT AAA AAC CAA GTG AAA GAA AAA TAC TCA TTT GTA     1293
Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr Ser Phe Val
340                 345                 350                 355

TCT GAA GTG GAA CCA AAT GAT ACT GAT CCA TTA GAT TCA AAT GTA GCA     1341
Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser Asn Val Ala
                360                 365                 370

CAT CAG AAG CCC TTT GAG AGT GGA AGT GAC AAA ATC TCC AAG GAA GTT     1389
His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser Lys Glu Val
            375                 380                 385

GTA CCG TCT TTG GCC TGT GAA TGG TCT CAA CTA ACC CTT TCA GGT CTA     1437
Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu Ser Gly Leu
        390                 395                 400
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AAT GGA GCC CAG ATG GAG AAA ATA CCC CTA TTG CAT ATT TCT TCA TGT    1485
Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile Ser Ser Cys
    405                 410                 415

GAC CAA AAT ATT TCA GAA AAA GAC CTA TTA GAC ACA GAG AAC AAA AGA    1533
Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu Asn Lys Arg
420                 425                 430                 435

AAG AAA GAT TTT CTT ACT TCA GAG AAT TCT TTG CCA CGT ATT TCT AGC    1581
Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg Ile Ser Ser
                440                 445                 450

CTA CCA AAA TCA GAG AAG CCA TTA AAT GAG GAA ACA GTG GTA AAT AAG    1629
Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val Val Asn Lys
            455                 460                 465

AGA GAT GAA GAG CAG CAT CTT GAA TCT CAT ACA GAC TGC ATT CTT GCA    1677
Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys Ile Leu Ala
        470                 475                 480

GTA AAG CAG GCA ATA TCT GGA ACT TCT CCA GTG GCT TCT TCA TTT CAG    1725
Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser Ser Phe Gln
    485                 490                 495

GGT ATC AAA AAG TCT ATA TTC AGA ATA AGA GAA TCA CCT AAA GAG ACT    1773
Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro Lys Glu Thr
500                 505                 510                 515

TTC AAT GCA AGT TTT TCA GGT CAT ATG ACT GAT CCA AAC TTT AAA AAA    1821
Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn Phe Lys Lys
                520                 525                 530

GAA ACT GAA GCC TCT GAA AGT GGA CTG GAA ATA CAT ACT GTT TGC TCA    1869
Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr Val Cys Ser
            535                 540                 545

CAG AAG GAG GAC TCC TTA TGT CCA AAT TTA ATT GAT AAT GGA AGC TGG    1917
Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn Gly Ser Trp
        550                 555                 560

CCA GCC ACC ACC ACA CAG AAT TCT GTA GCT TTG AAG AAT GCA GGT TTA    1965
Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn Ala Gly Leu
    565                 570                 575

ATA TCC ACT TTG AAA AAG AAA ACA AAT AAG TTT ATT TAT GCT ATA CAT    2013
Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr Ala Ile His
580                 585                 590                 595

GAT GAA ACA TCT TAT AAA GGA AAA AAA ATA CCG AAA GAC CAA AAA TCA    2061
Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp Gln Lys Ser
                600                 605                 610

GAA CTA ATT AAC TGT TCA GCC CAG TTT GAA GCA AAT GCT TTT GAA GCA    2109
Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala Phe Glu Ala
            615                 620                 625

CCA CTT ACA TTT GCA AAT GCT GAT TCA GGT TTA TTG CAT TCT TCT GTG    2157
Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His Ser Ser Val
        630                 635                 640

AAA AGA AGC TGT TCA CAG AAT GAT TCT GAA GAA CCA ACT TTG TCC TTA    2205
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Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr Leu Ser Leu
    645                 650                 655

ACT AGC TCT TTT GGG ACA ATT CTG AGG AAA TGT TCT AGA AAT GAA ACA    2253
Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg Asn Glu Thr
660                 665                 670                 675

TGT TCT AAT AAT ACA GTA ATC TCT CAG GAT CTT GAT TAT AAA GAA GCA    2301
Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr Lys Glu Ala
                680                 685                 690

AAA TGT AAT AAG GAA AAA CTA CAG TTA TTT ATT ACC CCA GAA GCT GAT    2349
Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro Glu Ala Asp
            695                 700                 705

TCT CTG TCA TGC CTG CAG GAA GGA CAG TGT GAA AAT GAT CCA AAA AGC    2397
Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp Pro Lys Ser
        710                 715                 720

AAA AAA GTT TCA GAT ATA AAA GAA GAG GTC TTG GCT GCA GCA TGT CAC    2445
Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala Ala Cys His
    725                 730                 735

CCA GTA CAA CAT TCA AAA GTG GAA TAC AGT GAT ACT GAC TTT CAA TCC    2493
Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp Phe Gln Ser
740                 745                 750                 755

CAG AAA AGT CTT TTA TAT GAT CAT GAA AAT GCC AGC ACT CTT ATT TTA    2541
Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr Leu Ile Leu
                760                 765                 770

ACT CCT ACT TCC AAG GAT GTT CTG TCA AAC CTA GTC ATG ATT TCT AGA    2589
Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met Ile Ser Arg
            775                 780                 785

GGC AAA GAA TCA TAC AAA ATG TCA GAC AAG CTC AAA GGT AAC AAT TAT    2637
Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly Asn Asn Tyr
        790                 795                 800

GAA TCT GAT GTT GAA TTA ACC AAA AAT ATT CCC ATG GAA AAG AAT CAA    2685
Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu Lys Asn Gln
    805                 810                 815

GAT GTA TGT GCT TTA AAT GAA AAT TAT AAA AAC GTT GAG CTG TTG CCA    2733
Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu Leu Leu Pro
820                 825                 830                 835

CCT GAA AAA TAC ATG AGA GTA GCA TCA CCT TCA AGA AAG GTA CAA TTC    2781
Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys Val Gln Phe
                840                 845                 850

AAC CAA AAC ACA AAT CTA AGA GTA ATC CAA AAA AAT CAA GAA GAA ACT    2829
Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln Glu Glu Thr
            855                 860                 865

ACT TCA ATT TCA AAA ATA ACT GTC AAT CCA GAC TCT GAA GAA CTT TTC    2877
Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu Glu Leu Phe
        870                 875                 880

TCA GAC AAT GAG AAT AAT TTT GTC TTC CAA GTA GCT AAT GAA AGG AAT    2925
Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn Glu Arg Asn
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          885                 890                 895

      AAT CTT GCT TTA GGA AAT ACT AAG GAA CTT CAT GAA ACA GAC TTG ACT    2973
 5    Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr Asp Leu Thr
      900                 905                 910                 915

      TGT GTA AAC GAA CCC ATT TTC AAG AAC TCT ACC ATG GTT TTA TAT GGA    3021
      Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val Leu Tyr Gly
10                    920                 925                 930

      GAC ACA GGT GAT AAA CAA GCA ACC CAA GTG TCA ATT AAA AAA GAT TTG    3069
      Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys Lys Asp Leu
                935                 940                 945
15
      GTT TAT GTT CTT GCA GAG GAG AAC AAA AAT AGT GTA AAG CAG CAT ATA    3117
      Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys Gln His Ile
           950                 955                 960

20    AAA ATG ACT CTA GGT CAA GAT TTA AAA TCG GAC ATC TCC TTG AAT ATA    3165
      Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser Leu Asn Ile
      965                 970                 975

      GAT AAA ATA CCA GAA AAA AAT AAT GAT TAC ATG AAC AAA TGG GCA GGA    3213
25    Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asn Lys Trp Ala Gly
      980                 985                 990                 995

      CTC TTA GGT CCA ATT TCA AAT CAC AGT TTT GGA GGT AGC TTC AGA ACA    3261
      Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser Phe Arg Thr
30                  1000                1005                1010

      GCT TCA AAT AAG GAA ATC AAG CTC TCT GAA CAT AAC ATT AAG AAG AGC    3309
      Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile Lys Lys Ser
               1015                1020                1025
35
      AAA ATG TTC TTC AAA GAT ATT GAA GAA CAA TAT CCT ACT AGT TTA GCT    3357
      Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr Ser Leu Ala
          1030                1035                1040

40    TGT GTT GAA ATT GTA AAT ACC TTG GCA TTA GAT AAT CAA AAG AAA CTG    3405
      Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln Lys Lys Leu
      1045                1050                1055

      AGC AAG CCT CAG TCA ATT AAT ACT GTA TCT GCA CAT TTA CAG AGT AGT    3453
45    Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu Gln Ser Ser
     1060                1065                1070                1075

      GTA GTT GTT TCT GAT TGT AAA AAT AGT CAT ATA ACC CCT CAG ATG TTA    3501
      Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro Gln Met Leu
50                  1080                1085                1090

      TTT TCC AAG CAG GAT TTT AAT TCA AAC CAT AAT TTA ACA CCT AGC CAA    3549
      Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr Pro Ser Gln
               1095                1100                1105
55
      AAG GCA GAA ATT ACA GAA CTT TCT ACT ATA TTA GAA GAA TCA GGA AGT    3597
      Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu Ser Gly Ser
          1110                1115                1120

60    CAG TTT GAA TTT ACT CAG TTT AGA AAA CCA AGC TAC ATA TTG CAG AAG    3645
      Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile Leu Gln Lys
      1125                1130                1135
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AGT ACA TTT GAA GTG CCT GAA AAC CAG ATG ACT ATC TTA AAG ACC ACT    3693
Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu Lys Thr Thr
1140                1145                1150                1155

TCT GAG GAA TGC AGA GAT GCT GAT CTT CAT GTC ATA ATG AAT GCC CCA    3741
Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met Asn Ala Pro
                1160                1165                1170

TCG ATT GGT CAG GTA GAC AGC AGC AAG CAA TTT GAA GGT ACA GTT GAA    3789
Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly Thr Val Glu
            1175                1180                1185

ATT AAA CGG AAG TTT GCT GGC CTG TTG AAA AAT GAC TGT AAC AAA AGT    3837
Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys Asn Lys Ser
        1190                1195                1200

GCT TCT GGT TAT TTA ACA GAT GAA AAT GAA GTG GGG TTT AGG GGC TTT    3885
Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe Arg Gly Phe
    1205                1210                1215

TAT TCT GCT CAT GGC ACA AAA CTG AAT GTT TCT ACT GAA GCT CTG CAA    3933
Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu Ala Leu Gln
1220                1225                1230                1235

AAA GCT GTG AAA CTG TTT AGT GAT ATT GAG AAT ATT AGT GAG GAA ACT    3981
Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser Glu Glu Thr
                1240                1245                1250

TCT GCA GAG GTA CAT CCA ATA AGT TTA TCT TCA AGT AAA TGT CAT GAT    4029
Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys Cys His Asp
            1255                1260                1265

TCT GTT GTT TCA ATG TTT AAG ATA GAA AAT CAT AAT GAT AAA ACT GTA    4077
Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp Lys Thr Val
        1270                1275                1280

AGT GAA AAA AAT AAT AAA TGC CAA CTG ATA TTA CAA AAT AAT ATT GAA    4125
Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn Asn Ile Glu
    1285                1290                1295

ATG ACT ACT GGC ACT TTT GTT GAA GAA ATT ACT GAA AAT TAC AAG AGA    4173
Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn Tyr Lys Arg
1300                1305                1310                1315

AAT ACT GAA AAT GAA GAT AAC AAA TAT ACT GCT GCC AGT AGA AAT TCT    4221
Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser Arg Asn Ser
                1320                1325                1330

CAT AAC TTA GAA TTT GAT GGC AGT GAT TCA AGT AAA AAT GAT ACT GTT    4269
His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn Asp Thr Val
            1335                1340                1345

TGT ATT CAT AAA GAT GAA ACG GAC TTG CTA TTT ACT GAT CAG CAC AAC    4317
Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp Gln His Asn
        1350                1355                1360

ATA TGT CTT AAA TTA TCT GGC CAG TTT ATG AAG GAG GGA AAC ACT CAG    4365
Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly Asn Thr Gln
    1365                1370                1375
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ATT AAA GAA GAT TTG TCA GAT TTA ACT TTT TTG GAA GTT GCG AAA GCT 4413
Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val Ala Lys Ala
1380 1385 1390 1395

CAA GAA GCA TGT CAT GGT AAT ACT TCA AAT AAA GAA CAG TTA ACT GCT 4461
Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln Leu Thr Ala
1400 1405 1410

ACT AAA ACG GAG CAA AAT ATA AAA GAT TTT GAG ACT TCT GAT ACA TTT 4509
Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser Asp Thr Phe
1415 1420 1425

TTT CAG ACT GCA AGT GGG AAA AAT ATT AGT GTC GCC AAA GAG TCA TTT 4557
Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys Glu Ser Phe
1430 1435 1440

AAT AAA ATT GTA AAT TTC TTT GAT CAG AAA CCA GAA GAA TTG CAT AAC 4605
Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu Leu His Asn
1445 1450 1455

TTT TCC TTA AAT TCT GAA TTA CAT TCT GAC ATA AGA AAG AAC AAA ATG 4653
Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys Asn Lys Met
1460 1465 1470 1475

GAC ATT CTA AGT TAT GAG GAA ACA GAC ATA GTT AAA CAC AAA ATA CTG 4701
Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His Lys Ile Leu
1480 1485 1490

AAA GAA AGT GTC CCA GTT GGT ACT GGA AAT CAA CTA GTG ACC TTC CAG 4749
Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val Thr Phe Gln
1495 1500 1505

GGA CAA CCC GAA CGT GAT GAA AAG ATC AAA GAA CCT ACT CTG TTG GGT 4797
Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr Leu Leu Gly
1510 1515 1520

TTT CAT ACA GCT AGC GGG AAA AAA GTT AAA ATT GCA AAG GAA TCT TTG 4845
Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys Glu Ser Leu
1525 1530 1535

GAC AAA GTG AAA AAC CTT TTT GAT GAA AAA GAG CAA GGT ACT AGT GAA 4893
Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly Thr Ser Glu
1540 1545 1550 1555

ATC ACC AGT TTT AGC CAT CAA TGG GCA AAG ACC CTA AAG TAC AGA GAG 4941
Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys Tyr Arg Glu
1560 1565 1570

GCC TGT AAA GAC CTT GAA TTA GCA TGT GAG ACC ATT GAG ATC ACA GCT 4989
Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu Ile Thr Ala
1575 1580 1585

GCC CCA AAG TGT AAA GAA ATG CAG AAT TCT CTC AAT AAT GAT AAA AAC 5037
Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn Asp Lys Asn
1590 1595 1600

CTT GTT TCT ATT GAG ACT GTG GTG CCA CCT AAG CTC TTA AGT GAT AAT 5085
Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu Ser Asp Asn
1605 1610 1615

TTA TGT AGA CAA ACT GAA AAT CTC AAA ACA TCA AAA AGT ATC TTT TTG 5133

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Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser Ile Phe Leu
1620                1625                1630                1635

AAA GTT AAA GTA CAT GAA AAT GTA GAA AAA GAA ACA GCA AAA AGT CCT    5181
Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala Lys Ser Pro
                1640                1645                1650

GCA ACT TGT TAC ACA AAT CAG TCC CCT TAT TCA GTC ATT GAA AAT TCA    5229
Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile Glu Asn Ser
            1655                1660                1665

GCC TTA GCT TTT TAC ACA AGT TGT AGT AGA AAA ACT TCT GTG AGT CAG    5277
Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser Val Ser Gln
        1670                1675                1680

ACT TCA TTA CTT GAA GCA AAA AAA TGG CTT AGA GAA GGA ATA TTT GAT    5325
Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly Ile Phe Asp
    1685                1690                1695

GGT CAA CCA GAA AGA ATA AAT ACT GCA GAT TAT GTA GGA AAT TAT TTG    5373
Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly Asn Tyr Leu
1700                1705                1710                1715

TAT GAA AAT AAT TCA AAC AGT ACT ATA GCT GAA AAT GAC AAA AAT CAT    5421
Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp Lys Asn His
                1720                1725                1730

CTC TCC GAA AAA CAA GAT ACT TAT TTA AGT AAC AGT AGC ATG TCT AAC    5469
Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser Met Ser Asn
            1735                1740                1745

AGC TAT TCC TAC CAT TCT GAT GAG GTA TAT AAT GAT TCA GGA TAT CTC    5517
Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser Gly Tyr Leu
        1750                1755                1760

TCA AAA AAT AAA CTT GAT TCT GGT ATT GAG CCA GTA TTG AAG AAT GTT    5565
Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu Lys Asn Val
    1765                1770                1775

GAA GAT CAA AAA AAC ACT AGT TTT TCC AAA GTA ATA TCC AAT GTA AAA    5613
Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser Asn Val Lys
1780                1785                1790                1795

GAT GCA AAT GCA TAC CCA CAA ACT GTA AAT GAA GAT ATT TGC GTT GAG    5661
Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile Cys Val Glu
                1800                1805                1810

GAA CTT GTG ACT AGC TCT TCA CCC TGC AAA AAT AAA AAT GCA GCC ATT    5709
Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn Ala Ala Ile
            1815                1820                1825

AAA TTG TCC ATA TCT AAT AGT AAT AAT TTT GAG GTA GGG CCA CCT GCA    5757
Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly Pro Pro Ala
        1830                1835                1840

TTT AGG ATA GCC AGT GGT AAA ATC GTT TGT GTT TCA CAT GAA ACA ATT    5805
Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His Glu Thr Ile
    1845                1850                1855

AAA AAA GTG AAA GAC ATA TTT ACA GAC AGT TTC AGT AAA GTA ATT AAG    5853
Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys Val Ile Lys
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1860                1865                1870                1875

 GAA AAC AAC GAG AAT AAA TCA AAA ATT TGC CAA ACG AAA ATT ATG GCA    5901
 Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys Ile Met Ala
                1880                1885                1890

 GGT TGT TAC GAG GCA TTG GAT GAT TCA GAG GAT ATT CTT CAT AAC TCT    5949
 Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu His Asn Ser
            1895                1900                1905

 CTA GAT AAT GAT GAA TGT AGC ACG CAT TCA CAT AAG GTT TTT GCT GAC    5997
 Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val Phe Ala Asp
        1910                1915                1920

 ATT CAG AGT GAA GAA ATT TTA CAA CAT AAC CAA AAT ATG TCT GGA TTG    6045
 Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met Ser Gly Leu
    1925                1930                1935

 GAG AAA GTT TCT AAA ATA TCA CCT TGT GAT GTT AGT TTG GAA ACT TCA    6093
 Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu Glu Thr Ser
1940                1945                1950                1955

 GAT ATA TGT AAA TGT AGT ATA GGG AAG CTT CAT AAG TCA GTC TCA TCT    6141
 Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser Val Ser Ser
                1960                1965                1970

 GCA AAT ACT TGT GGG ATT TTT AGC ACA GCA AGT GGA AAA TCT GTC CAG    6189
 Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys Ser Val Gln
            1975                1980                1985

 GTA TCA GAT GCT TCA TTA CAA AAC GCA AGA CAA GTG TTT TCT GAA ATA    6237
 Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe Ser Glu Ile
        1990                1995                2000

 GAA GAT AGT ACC AAG CAA GTC TTT TCC AAA GTA TTG TTT AAA AGT AAC    6285
 Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe Lys Ser Asn
    2005                2010                2015

 GAA CAT TCA GAC CAG CTC ACA AGA GAA GAA AAT ACT GCT ATA CGT ACT    6333
 Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala Ile Arg Thr
2020                2025                2030                2035

 CCA GAA CAT TTA ATA TCC CAA AAA GGC TTT TCA TAT AAT GTG GTA AAT    6381
 Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn Val Val Asn
                2040                2045                2050

 TCA TCT GCT TTC TCT GGA TTT AGT ACA GCA AGT GGA AAG CAA GTT TCC    6429
 Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys Gln Val Ser
            2055                2060                2065

 ATT TTA GAA AGT TCC TTA CAC AAA GTT AAG GGA GTG TTA GAG GAA TTT    6477
 Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu Glu Glu Phe
        2070                2075                2080

 GAT TTA ATC AGA ACT GAG CAT AGT CTT CAC TAT TCA CCT ACG TCT AGA    6525
 Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro Thr Ser Arg
    2085                2090                2095

 CAA AAT GTA TCA AAA ATA CTT CCT CGT GTT GAT AAG AGA AAC CCA GAG    6573
 Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg Asn Pro Glu
2100                2105                2110                2115
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CAC TGT GTA AAC TCA GAA ATG GAA AAA ACC TGC AGT AAA GAA TTT AAA 6621
His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys Glu Phe Lys
2120 2125 2130

TTA TCA AAT AAC TTA AAT GTT GAA GGT GGT TCT TCA GAA AAT AAT CAC 6669
Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu Asn Asn His
2135 2140 2145

TCT ATT AAA GTT TCT CCA TAT CTC TCT CAA TTT CAA CAA GAC AAA CAA 6717
Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln Asp Lys Gln
2150 2155 2160

CAG TTG GTA TTA GGA ACC AAA GTC TCA CTT GTT GAG AAC ATT CAT GTT 6765
Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn Ile His Val
2165 2170 2175

TTG GGA AAA GAA CAG GCT TCA CCT AAA AAC GTA AAA ATG GAA ATT GGT 6813
Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met Glu Ile Gly
2180 2185 2190 2195

AAA ACT GAA ACT TTT TCT GAT GTT CCT GTG AAA ACA AAT ATA GAA GTT 6861
Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn Ile Glu Val
2200 2205 2210

TGT TCT ACT TAC TCC AAA GAT TCA GAA AAC TAC TTT GAA ACA GAA GCA 6909
Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu Thr Glu Ala
2215 2220 2225

GTA GAA ATT GCT AAA GCT TTT ATG GAA GAT GAT GAA CTG ACA GAT TCT 6957
Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu Thr Asp Ser
2230 2235 2240

AAA CTG CCA AGT CAT GCC ACA CAT TCT CTT TTT ACA TGT CCC GAA AAT 7005
Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys Pro Glu Asn
2245 2250 2255

GAG GAA ATG GTT TTG TCA AAT TCA AGA ATT GGA AAA AGA AGA GGA GAG 7053
Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg Arg Gly Glu
2260 2265 2270 2275

CCC CTT ATC TTA GTG GGA GAA CCC TCA ATC AAA AGA AAC TTA TTA AAT 7101
Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn Leu Leu Asn
2280 2285 2290

GAA TTT GAC AGG ATA ATA GAA AAT CAA GAA AAA TCC TTA AAG GCT TCA 7149
Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu Lys Ala Ser
2295 2300 2305

AAA AGC ACT CCA GAT GGC ACA ATA AAA GAT CGA AGA TTG TTT ATG CAT 7197
Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu Phe Met His
2310 2315 2320

CAT GTT TCT TTA GAG CCG ATT ACC TGT GTA CCC TTT CGC ACA ACT AAG 7245
His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg Thr Thr Lys
2325 2330 2335

GAA CGT CAA GAG ATA CAG AAT CCA AAT TTT ACC GCA CCT GGT CAA GAA 7293
Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro Gly Gln Glu
2340 2345 2350 2355

TTT CTG TCT AAA TCT CAT TTG TAT GAA CAT CTG ACT TTG GAA AAA TCT 7341
Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu Glu Lys Ser
2360 2365 2370

TCA AGC AAT TTA GCA GTT TCA GGA CAT CCA TTT TAT CAA GTT TCT GCT 7389
Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln Val Ser Ala
2375 2380 2385

ACA AGA AAT GAA AAA ATG AGA CAC TTG ATT ACT ACA GGC AGA CCA ACC 7437
Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly Arg Pro Thr
2390 2395 2400

AAA GTC TTT GTT CCA CCT TTT AAA ACT AAA TCA CAT TTT CAC AGA GTT 7485
Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe His Arg Val
2405 2410 2415

GAA CAG TGT GTT AGG AAT ATT AAC TTG GAG GAA AAC AGA CAA AAG CAA 7533
Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg Gln Lys Gln
2420 2425 2430 2435

AAC ATT GAT GGA CAT GGC TCT GAT GAT AGT AAA AAT AAG ATT AAT GAC 7581
Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys Ile Asn Asp
2440 2445 2450

AAT GAG ATT CAT CAG TTT AAC AAA AAC AAC TCC AAT CAA GCA GCA GCT 7629
Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln Ala Ala Ala
2455 2460 2465

GTA ACT TTC ACA AAG TGT GAA GAA GAA CCT TTA GAT TTA ATT ACA AGT 7677
Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu Ile Thr Ser
2470 2475 2480

CTT CAG AAT GCC AGA GAT ATA CAG GAT ATG CGA ATT AAG AAG AAA CAA 7725
Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys Lys Lys Gln
2485 2490 2495

AGG CAA CGC GTC TTT CCA CAG CCA GGC AGT CTG TAT CTT GCA AAA ACA 7773
Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu Ala Lys Thr
2500 2505 2510 2515

TCC ACT CTG CCT CGA ATC TCT CTG AAA GCA GCA GTA GGA GGC CAA GTT 7821
Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly Gly Gln Val
2520 2525 2530

CCC TCT GCG TGT TCT CAT AAA CAG CTG TAT ACG TAT GGC GTT TCT AAA 7869
Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly Val Ser Lys
2535 2540 2545

CAT TGC ATA AAA ATT AAC AGC AAA AAT GCA GAG TCT TTT CAG TTT CAC 7917
His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe Gln Phe His
2550 2555 2560

ACT GAA GAT TAT TTT GGT AAG GAA AGT TTA TGG ACT GGA AAA GGA ATA 7965
Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly Lys Gly Ile
2565 2570 2575

CAG TTG GCT GAT GGT GGA TGG CTC ATA CCC TCC AAT GAT GGA AAG GCT 8013
Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp Gly Lys Ala
2580 2585 2590 2595

GGA AAA GAA GAA TTT TAT AGG GCT CTG TGT GAC ACT CCA GGT GTG GAT 8061

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Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro Gly Val Asp
                2600                2605                2610

CCA AAG CTT ATT TCT AGA ATT TGG GTT TAT AAT CAC TAT AGA TGG ATC    8109
Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr Arg Trp Ile
            2615                2620                2625

ATA TGG AAA CTG GCA GCT ATG GAA TGT GCC TTT CCT AAG GAA TTT GCT    8157
Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys Glu Phe Ala
        2630                2635                2640

AAT AGA TGC CTA AGC CCA GAA AGG GTG CTT CTT CAA CTA AAA TAC AGA    8205
Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu Lys Tyr Arg
    2645                2650                2655

TAT GAT ACG GAA ATT GAT AGA AGC AGA AGA TCG GCT ATA AAA AAG ATA    8253
Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile Lys Lys Ile
2660                2665                2670                2675

ATG GAA AGG GAT GAC ACA GCT GCA AAA ACA CTT GTT CTC TGT GTT TCT    8301
Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu Cys Val Ser
                2680                2685                2690

GAC ATA ATT TCA TTG AGC GCA AAT ATA TCT GAA ACT TCT AGC AAT AAA    8349
Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser Ser Asn Lys
            2695                2700                2705

ACT AGT AGT GCA GAT ACC CAA AAA GTG GCC ATT ATT GAA CTT ACA GAT    8397
Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu Leu Thr Asp
        2710                2715                2720

GGG TGG TAT GCT GTT AAG GCC CAG TTA GAT CCT CCC CTC TTA GCT GTC    8445
Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu Leu Ala Val
    2725                2730                2735

TTA AAG AAT GGC AGA CTG ACA GTT GGT CAG AAG ATT ATT CTT CAT GGA    8493
Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile Leu His Gly
2740                2745                2750                2755

GCA GAA CTG GTG GGC TCT CCT GAT GCC TGT ACA CCT CTT GAA GCC CCA    8541
Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu Glu Ala Pro
                2760                2765                2770

GAA TCT CTT ATG TTA AAG ATT TCT GCT AAC AGT ACT CGG CCT GCT CGC    8589
Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg Pro Ala Arg
            2775                2780                2785

TGG TAT ACC AAA CTT GGA TTC TTT CCT GAC CCT AGA CCT TTT CCT CTG    8637
Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro Phe Pro Leu
        2790                2795                2800

CCC TTA TCA TCG CTT TTC AGT GAT GGA GGA AAT GTT GGT TGT GTT GAT    8685
Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly Cys Val Asp
    2805                2810                2815

GTA ATT ATT CAA AGA GCA TAC CCT ATA CAG TGG ATG GAG AAG ACA TCA    8733
Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu Lys Thr Ser
2820                2825                2830                2835

TCT GGA TTA TAC ATA TTT CGC AAT GAA AGA GAG GAA GAA AAG GAA GCA    8781
Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu Lys Glu Ala
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                    2840                2845                2850

     GCA AAA TAT GTG GAG GCC CAA CAA AAG AGA CTA GAA GCC TTA TTC ACT    8829
5    Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala Leu Phe Thr
               2855                2860                2865

     AAA ATT CAG GAG GAA TTT GAA GAA CAT GAA GAA AAC ACA ACA AAA CCA    8877
     Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr Thr Lys Pro
10         2870                2875                2880

     TAT TTA CCA TCA CGT GCA CTA ACA AGA CAG CAA GTT CGT GCT TTG CAA    8925
     Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg Ala Leu Gln
     2885                2890                2895
15
     GAT GGT GCA GAG CTT TAT GAA GCA GTG AAG AAT GCA GCA GAC CCA GCT    8973
     Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala Asp Pro Ala
2900                2905                2910                2915

20   TAC CTT GAG GGT TAT TTC AGT GAA GAG CAG TTA AGA GCC TTG AAT AAT    9021
     Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala Leu Asn Asn
                    2920                2925                2930

     CAC AGG CAA ATG TTG AAT GAT AAG AAA CAA GCT CAG ATC CAG TTG GAA    9069
25   His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile Gln Leu Glu
               2935                2940                2945

     ATT AGG AAG GCC ATG GAA TCT GCT GAA CAA AAG GAA CAA GGT TTA TCA    9117
     Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln Gly Leu Ser
30         2950                2955                2960

     AGG GAT GTC ACA ACC GTG TGG AAG TTG CGT ATT GTA AGC TAT TCA AAA    9165
     Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser Tyr Ser Lys
     2965                2970                2975
35
     AAA GAA AAA GAT TCA GTT ATA CTG AGT ATT TGG CGT CCA TCA TCA GAT    9213
     Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro Ser Ser Asp
2980                2985                2990                2995

40   TTA TAT TCT CTG TTA ACA GAA GGA AAG AGA TAC AGA ATT TAT CAT CTT    9261
     Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile Tyr His Leu
                    3000                3005                3010

     GCA ACT TCA AAA TCT AAA AGT AAA TCT GAA AGA GCT AAC ATA CAG TTA    9309
45   Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn Ile Gln Leu
               3015                3020                3025

     GCA GCG ACA AAA AAA ACT CAG TAT CAA CAA CTA CCG GTT TCA GAT GAA    9357
     Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val Ser Asp Glu
50         3030                3035                3040

     ATT TTA TTT CAG ATT TAC CAG CCA CGG GAG CCC CTT CAC TTC AGC AAA    9405
     Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His Phe Ser Lys
     3045                3050                3055
55
     TTT TTA GAT CCA GAC TTT CAG CCA TCT TGT TCT GAG GTG GAC CTA ATA    9453
     Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val Asp Leu Ile
3060                3065                3070                3075

60   GGA TTT GTC GTT TCT GTT GTG AAA AAA ACA GGA CTT GCC CCT TTC GTC    9501
     Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala Pro Phe Val
                    3080                3085                3090
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TAT TTG TCA GAC GAA TGT TAC AAT TTA CTG GCA ATA AAG TTT TGG ATA    9549
Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys Phe Trp Ile
            3095                3100                3105

GAC CTT AAT GAG GAC ATT ATT AAG CCT CAT ATG TTA ATT GCT GCA AGC    9597
Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile Ala Ala Ser
        3110                3115                3120

AAC CTC CAG TGG CGA CCA GAA TCC AAA TCA GGC CTT CTT ACT TTA TTT    9645
Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu Thr Leu Phe
    3125                3130                3135

GCT GGA GAT TTT TCT GTG TTT TCT GCT AGT CCA AAA GAG GGC CAC TTT    9693
Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu Gly His Phe
3140                3145                3150                3155

CAA GAG ACA TTC AAC AAA ATG AAA AAT ACT GTT GAG AAT ATT GAC ATA    9741
Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn Ile Asp Ile
                3160                3165                3170

CTT TGC AAT GAA GCA GAA AAC AAG CTT ATG CAT ATA CTG CAT GCA AAT    9789
Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu His Ala Asn
            3175                3180                3185

GAT CCC AAG TGG TCC ACC CCA ACT AAA GAC TGT ACT TCA GGG CCG TAC    9837
Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser Gly Pro Tyr
        3190                3195                3200

ACT GCT CAA ATC ATT CCT GGT ACA GGA AAC AAG CTT CTG ATG TCT TCT    9885
Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu Met Ser Ser
    3205                3210                3215

CCT AAT TGT GAG ATA TAT TAT CAA AGT CCT TTA TCA CTT TGT ATG GCC    9933
Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu Cys Met Ala
3220                3225                3230                3235

AAA AGG AAG TCT GTT TCC ACA CCT GTC TCA GCC CAG ATG ACT TCA AAG    9981
Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met Thr Ser Lys
                3240                3245                3250

TCT TGT AAA GGG GAG AAA GAG ATT GAT GAC CAA AAG AAC TGC AAA AAG   10029
Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn Cys Lys Lys
            3255                3260                3265

AGA AGA GCC TTG GAT TTC TTG AGT AGA CTG CCT TTA CCT CCA CCT GTT   10077
Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro Pro Pro Val
        3270                3275                3280

AGT CCC ATT TGT ACA TTT GTT TCT CCG GCT GCA CAG AAG GCA TTT CAG   10125
Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys Ala Phe Gln
    3285                3290                3295

CCA CCA AGG AGT TGT GGC ACC AAA TAC GAA ACA CCC ATA AAG AAA AAA   10173
Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile Lys Lys Lys
3300                3305                3310                3315

GAA CTG AAT TCT CCT CAG ATG ACT CCA TTT AAA AAA TTC AAT GAA ATT   10221
Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe Asn Glu Ile
                3320                3325                3330
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TCT CTT TTG GAA AGT AAT TCA ATA GCT GAC GAA GAA CTT GCA TTG ATA   10269
Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile
          3335                3340                3345

AAT ACC CAA GCT CTT TTG TCT GGT TCA ACA GGA GAA AAA CAA TTT ATA   10317
Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys Gln Phe Ile
      3350                3355                3360

TCT GTC AGT GAA TCC ACT AGG ACT GCT CCC ACC AGT TCA GAA GAT TAT   10365
Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp Tyr
   3365                3370                3375

CTC AGA CTG AAA CGA CGT TGT ACT ACA TCT CTG ATC AAA GAA CAG GAG   10413
Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu Gln Glu
3380                3385                3390                3395

AGT TCC CAG GCC AGT ACG GAA GAA TGT GAG AAA AAT AAG CAG GAC ACA   10461
Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys Gln Asp Thr
               3400                3405                3410

ATT ACA ACT AAA AAA TAT ATC TAA                                  10485
Ile Thr Thr Lys Lys Tyr Ile
          3415
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(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 3418 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

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Met Pro Ile Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys
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Thr Arg Cys Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe
            20                  25                  30
Glu Glu Leu Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu
        35                  40                  45
Glu Ser Glu His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr
    50                  55                  60
Pro Gln Arg Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile
65                  70                  75                  80
Phe Lys Glu Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys
                85                  90                  95
Glu Leu Asp Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser
            100                 105                 110
Arg His Lys Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp
        115                 120                 125
Asp Val Ser Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val
    130                 135                 140
Val Leu Gln Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val
145                 150                 155                 160
Cys Gly Ser Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr
                165                 170                 175
Pro Lys His Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met
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                180                 185                 190
Ser Trp Ser Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val
        195                 200                 205
Leu Ile Val Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp
    210                 215                 220
Thr Thr Ala Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu
225                 230                 235                 240
Lys Lys Asn Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr
                245                 250                 255
Asn Gln Arg Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn
            260                 265                 270
Ser Phe Lys Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro
        275                 280                 285
Asn Val Leu Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu
    290                 295                 300
Glu Asp Ser Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu
305                 310                 315                 320
Gln Lys Val Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala
                325                 330                 335
Asn Ala Asp Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr
            340                 345                 350
Ser Phe Val Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser
        355                 360                 365
Asn Val Ala His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser
    370                 375                 380
Lys Glu Val Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu
385                 390                 395                 400
Ser Gly Leu Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile
                405                 410                 415
Ser Ser Cys Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu
            420                 425                 430
Asn Lys Arg Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg
        435                 440                 445
Ile Ser Ser Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val
    450                 455                 460
Val Asn Lys Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys
465                 470                 475                 480
Ile Leu Ala Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser
                485                 490                 495
Ser Phe Gln Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro
            500                 505                 510
Lys Glu Thr Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn
        515                 520                 525
Phe Lys Lys Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr
    530                 535                 540
Val Cys Ser Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn
545                 550                 555                 560
Gly Ser Trp Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn
                565                 570                 575
Ala Gly Leu Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr
            580                 585                 590
Ala Ile His Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp
        595                 600                 605
Gln Lys Ser Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala
    610                 615                 620
Phe Glu Ala Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His
625                 630                 635                 640
Ser Ser Val Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr
                645                 650                 655
Leu Ser Leu Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg
            660                 665                 670
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Asn Glu Thr Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr
675 680 685
Lys Glu Ala Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro
690 695 700
Glu Ala Asp Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp
705 710 715 720
Pro Lys Ser Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala
725 730 735
Ala Cys His Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp
740 745 750
Phe Gln Ser Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr
755 760 765
Leu Ile Leu Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met
770 775 780
Ile Ser Arg Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly
785 790 795 800
Asn Asn Tyr Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu
805 810 815
Lys Asn Gln Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu
820 825 830
Leu Leu Pro Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys
835 840 845
Val Gln Phe Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln
850 855 860
Glu Glu Thr Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu
865 870 875 880
Glu Leu Phe Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn
885 890 895
Glu Arg Asn Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr
900 905 910
Asp Leu Thr Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val
915 920 925
Leu Tyr Gly Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys
930 935 940
Lys Asp Leu Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys
945 950 955 960
Gln His Ile Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser
965 970 975
Leu Asn Ile Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asn Lys
980 985 990
Trp Ala Gly Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser
995 1000 1005
Phe Arg Thr Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile
1010 1015 1020
Lys Lys Ser Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr
1025 1030 1035 104
Ser Leu Ala Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln
1045 1050 1055
Lys Lys Leu Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu
1060 1065 1070
Gln Ser Ser Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro
1075 1080 1085
Gln Met Leu Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr
1090 1095 1100
Pro Ser Gln Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu
1105 1110 1115 112
Ser Gly Ser Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile
1125 1130 1135
Leu Gln Lys Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu
1140 1145 1150
Lys Thr Thr Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met

1155 1160 1165

Asn Ala Pro Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly
1170 1175 1180

Thr Val Glu Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys
1185 1190 1195 120

Asn Lys Ser Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe
1205 1210 1215

Arg Gly Phe Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu
1220 1225 1230

Ala Leu Gln Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser
1235 1240 1245

Glu Glu Thr Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys
1250 1255 1260

Cys His Asp Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp
1265 1270 1275 128

Lys Thr Val Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn
1285 1290 1295

Asn Ile Glu Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn
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Tyr Lys Arg Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser
1315 1320 1325

Arg Asn Ser His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn
1330 1335 1340

Asp Thr Val Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp
1345 1350 1355 136

Gln His Asn Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly
1365 1370 1375

Asn Thr Gln Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val
1380 1385 1390

Ala Lys Ala Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln
1395 1400 1405

Leu Thr Ala Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser
1410 1415 1420

Asp Thr Phe Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys
1425 1430 1435 144

Glu Ser Phe Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu
1445 1450 1455

Leu His Asn Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys
1460 1465 1470

Asn Lys Met Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His
1475 1480 1485

Lys Ile Leu Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val
1490 1495 1500

Thr Phe Gln Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr
1505 1510 1515 152

Leu Leu Gly Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys
1525 1530 1535

Glu Ser Leu Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly
1540 1545 1550

Thr Ser Glu Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys
1555 1560 1565

Tyr Arg Glu Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu
1570 1575 1580

Ile Thr Ala Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn
1585 1590 1595 160

Asp Lys Asn Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu
1605 1610 1615

Ser Asp Asn Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser
1620 1625 1630

Ile Phe Leu Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala
1635 1640 1645

Lys Ser Pro Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile
1650 1655 1660
Glu Asn Ser Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser
1665 1670 1675 168
Val Ser Gln Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly
1685 1690 1695
Ile Phe Asp Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly
1700 1705 1710
Asn Tyr Leu Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp
1715 1720 1725
Lys Asn His Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser
1730 1735 1740
Met Ser Asn Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser
1745 1750 1755 176
Gly Tyr Leu Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu
1765 1770 1775
Lys Asn Val Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser
1780 1785 1790
Asn Val Lys Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile
1795 1800 1805
Cys Val Glu Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn
1810 1815 1820
Ala Ala Ile Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly
1825 1830 1835 184
Pro Pro Ala Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His
1845 1850 1855
Glu Thr Ile Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys
1860 1865 1870
Val Ile Lys Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys
1875 1880 1885
Ile Met Ala Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu
1890 1895 1900
His Asn Ser Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val
1905 1910 1915 192
Phe Ala Asp Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met
1925 1930 1935
Ser Gly Leu Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu
1940 1945 1950
Glu Thr Ser Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser
1955 1960 1965
Val Ser Ser Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys
1970 1975 1980
Ser Val Gln Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe
1985 1990 1995 200
Ser Glu Ile Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe
2005 2010 2015
Lys Ser Asn Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala
2020 2025 2030
Ile Arg Thr Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn
2035 2040 2045
Val Val Asn Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys
2050 2055 2060
Gln Val Ser Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu
2065 2070 2075 208
Glu Glu Phe Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro
2085 2090 2095
Thr Ser Arg Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg
2100 2105 2110
Asn Pro Glu His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys
2115 2120 2125
Glu Phe Lys Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu

2130 2135 2140
Asn Asn His Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln
2145 2150 2155 216
Asp Lys Gln Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn
2165 2170 2175
Ile His Val Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met
2180 2185 2190
Glu Ile Gly Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn
2195 2200 2205
Ile Glu Val Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu
2210 2215 2220
Thr Glu Ala Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu
2225 2230 2235 224
Thr Asp Ser Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys
2245 2250 2255
Pro Glu Asn Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg
2260 2265 2270
Arg Gly Glu Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn
2275 2280 2285
Leu Leu Asn Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu
2290 2295 2300
Lys Ala Ser Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu
2305 2310 2315 232
Phe Met His His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg
2325 2330 2335
Thr Thr Lys Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro
2340 2345 2350
Gly Gln Glu Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu
2355 2360 2365
Glu Lys Ser Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln
2370 2375 2380
Val Ser Ala Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly
2385 2390 2395 240
Arg Pro Thr Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe
2405 2410 2415
His Arg Val Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg
2420 2425 2430
Gln Lys Gln Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys
2435 2440 2445
Ile Asn Asp Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln
2450 2455 2460
Ala Ala Ala Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu
2465 2470 2475 248
Ile Thr Ser Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys
2485 2490 2495
Lys Lys Gln Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu
2500 2505 2510
Ala Lys Thr Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly
2515 2520 2525
Gly Gln Val Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly
2530 2535 2540
Val Ser Lys His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe
2545 2550 2555 256
Gln Phe His Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly
2565 2570 2575
Lys Gly Ile Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp
2580 2585 2590
Gly Lys Ala Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro
2595 2600 2605
Gly Val Asp Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr
2610 2615 2620

Arg Trp Ile Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys
2625 2630 2635 264
Glu Phe Ala Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu
2645 2650 2655
Lys Tyr Arg Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile
2660 2665 2670
Lys Lys Ile Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu
2675 2680 2685
Cys Val Ser Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser
2690 2695 2700
Ser Asn Lys Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu
2705 2710 2715 272
Leu Thr Asp Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu
2725 2730 2735
Leu Ala Val Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile
2740 2745 2750
Leu His Gly Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu
2755 2760 2765
Glu Ala Pro Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg
2770 2775 2780
Pro Ala Arg Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro
2785 2790 2795 280
Phe Pro Leu Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly
2805 2810 2815
Cys Val Asp Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu
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Lys Thr Ser Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu
2835 2840 2845
Lys Glu Ala Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala
2850 2855 2860
Leu Phe Thr Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr
2865 2870 2875 288
Thr Lys Pro Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg
2885 2890 2895
Ala Leu Gln Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala
2900 2905 2910
Asp Pro Ala Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala
2915 2920 2925
Leu Asn Asn His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile
2930 2935 2940
Gln Leu Glu Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln
2945 2950 2955 296
Gly Leu Ser Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser
2965 2970 2975
Tyr Ser Lys Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro
2980 2985 2990
Ser Ser Asp Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile
2995 3000 3005
Tyr His Leu Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn
3010 3015 3020
Ile Gln Leu Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val
3025 3030 3035 304
Ser Asp Glu Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His
3045 3050 3055
Phe Ser Lys Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val
3060 3065 3070
Asp Leu Ile Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala
3075 3080 3085
Pro Phe Val Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys
3090 3095 3100
Phe Trp Ile Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile

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3105                 3110                 3115                 312
Ala Ala Ser Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu
                  3125                 3130                 3135
Thr Leu Phe Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu
               3140                 3145                 3150
Gly His Phe Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn
         3155                 3160                 3165
Ile Asp Ile Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu
     3170                 3175                 3180
His Ala Asn Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser
3185                 3190                 3195                 320
Gly Pro Tyr Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu
                  3205                 3210                 3215
Met Ser Ser Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu
               3220                 3225                 3230
Cys Met Ala Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met
         3235                 3240                 3245
Thr Ser Lys Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn
     3250                 3255                 3260
Cys Lys Lys Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro
3265                 3270                 3275                 328
Pro Pro Val Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys
                  3285                 3290                 3295
Ala Phe Gln Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile
               3300                 3305                 3310
Lys Lys Lys Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe
         3315                 3320                 3325
Asn Glu Ile Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu
     3330                 3335                 3340
Ala Leu Ile Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys
3345                 3350                 3355                 336
Gln Phe Ile Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser
                  3365                 3370                 3375
Glu Asp Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys
               3380                 3385                 3390
Glu Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys
         3395                 3400                 3405
Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile
     3410                 3415
```

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10485 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 229...10482
(D) OTHER INFORMATION: BRCA2 (OMI2)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

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GGTGGCGCGA GCTTCTGAAA CTAGGCGGCA GAGGCGGAGC CGCTGTGGCA CTGCTGCGCC     60
TCTGCTGCGC CTCGGGTGTC TTTTGCGGCG GTGGGTCGCC GCCGGGAGAA GCGTGAGGGG    120
ACAGATTTGT GACCGGCGCG GTTTTTGTCA GCTTACTCCG GCCAAAAAAG AACTGCACCT    180
CTGGAGCGGA CTTATTTACC AAGCATTGGA GGAATATCGT AGGTAAAA ATG CCT ATT    237
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                                                                Met Pro Ile
                                                                 1

GGA TCC AAA GAG AGG CCA ACA TTT TTT GAA ATT TTT AAG ACA CGC TGC      285
Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys Thr Arg Cys
     5                  10                  15

AAC AAA GCA GAT TTA GGA CCA ATA AGT CTT AAT TGG TTT GAA GAA CTT      333
Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe Glu Glu Leu
20                  25                  30                  35

TCT TCA GAA GCT CCA CCC TAT AAT TCT GAA CCT GCA GAA GAA TCT GAA      381
Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu Glu Ser Glu
                40                  45                  50

CAT AAA AAC AAC AAT TAC GAA CCA AAC CTA TTT AAA ACT CCA CAA AGG      429
His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr Pro Gln Arg
            55                  60                  65

AAA CCA TCT TAT AAT CAG CTG GCT TCA ACT CCA ATA ATA TTC AAA GAG      477
Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile Phe Lys Glu
        70                  75                  80

CAA GGG CTG ACT CTG CCG CTG TAC CAA TCT CCT GTA AAA GAA TTA GAT      525
Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys Glu Leu Asp
    85                  90                  95

AAA TTC AAA TTA GAC TTA GGA AGG AAT GTT CCC AAT AGT AGA CAT AAA      573
Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser Arg His Lys
100                 105                 110                 115

AGT CTT CGC ACA GTG AAA ACT AAA ATG GAT CAA GCA GAT GAT GTT TCC      621
Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp Asp Val Ser
                120                 125                 130

TGT CCA CTT CTA AAT TCT TGT CTT AGT GAA AGT CCT GTT GTT CTA CAA      669
Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val Val Leu Gln
            135                 140                 145

TGT ACA CAT GTA ACA CCA CAA AGA GAT AAG TCA GTG GTA TGT GGG AGT      717
Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val Cys Gly Ser
        150                 155                 160

TTG TTT CAT ACA CCA AAG TTT GTG AAG GGT CGT CAG ACA CCA AAA CAT      765
Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr Pro Lys His
    165                 170                 175

ATT TCT GAA AGT CTA GGA GCT GAG GTG GAT CCT GAT ATG TCT TGG TCA      813
Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met Ser Trp Ser
180                 185                 190                 195

AGT TCT TTA GCT ACA CCA CCC ACC CTT AGT TCT ACT GTG CTC ATA GTC      861
Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val Leu Ile Val
                200                 205                 210

AGA AAT GAA GAA GCA TCT GAA ACT GTA TTT CCT CAT GAT ACT ACT GCT      909
Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp Thr Thr Ala
            215                 220                 225

AAT GTG AAA AGC TAT TTT TCC AAT CAT GAT GAA AGT CTG AAG AAA AAT      957
Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu Lys Lys Asn
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                230                 235                 240

     GAT AGA TTT ATC GCT TCT GTG ACA GAC AGT GAA AAC ACA AAT CAA AGA    1005
 5   Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr Asn Gln Arg
         245                 250                 255

     GAA GCT GCA AGT CAT GGA TTT GGA AAA ACA TCA GGG AAT TCA TTT AAA    1053
     Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn Ser Phe Lys
10   260                 265                 270                 275

     GTA AAT AGC TGC AAA GAC CAC ATT GGA AAG TCA ATG CCA AAT GTC CTA    1101
     Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro Asn Val Leu
                     280                 285                 290
15
     GAA GAT GAA GTA TAT GAA ACA GTT GTA GAT ACC TCT GAA GAA GAT AGT    1149
     Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu Glu Asp Ser
                 295                 300                 305

20   TTT TCA TTA TGT TTT TCT AAA TGT AGA ACA AAA AAT CTA CAA AAA GTA    1197
     Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu Gln Lys Val
             310                 315                 320

     AGA ACT AGC AAG ACT AGG AAA AAA ATT TTC CAT GAA GCA AAC GCT GAT    1245
25   Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala Asn Ala Asp
         325                 330                 335

     GAA TGT GAA AAA TCT AAA AAC CAA GTG AAA GAA AAA TAC TCA TTT GTA    1293
     Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr Ser Phe Val
30   340                 345                 350                 355

     TCT GAA GTG GAA CCA AAT GAT ACT GAT CCA TTA GAT TCA AAT GTA GCA    1341
     Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser Asn Val Ala
                     360                 365                 370
35
     CAT CAG AAG CCC TTT GAG AGT GGA AGT GAC AAA ATC TCC AAG GAA GTT    1389
     His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser Lys Glu Val
                 375                 380                 385

40   GTA CCG TCT TTG GCC TGT GAA TGG TCT CAA CTA ACC CTT TCA GGT CTA    1437
     Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu Ser Gly Leu
             390                 395                 400

     AAT GGA GCC CAG ATG GAG AAA ATA CCC CTA TTG CAT ATT TCT TCA TGT    1485
45   Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile Ser Ser Cys
         405                 410                 415

     GAC CAA AAT ATT TCA GAA AAA GAC CTA TTA GAC ACA GAG AAC AAA AGA    1533
     Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu Asn Lys Arg
50   420                 425                 430                 435

     AAG AAA GAT TTT CTT ACT TCA GAG AAT TCT TTG CCA CGT ATT TCT AGC    1581
     Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg Ile Ser Ser
                     440                 445                 450
55
     CTA CCA AAA TCA GAG AAG CCA TTA AAT GAG GAA ACA GTG GTA AAT AAG    1629
     Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val Val Asn Lys
                 455                 460                 465

60   AGA GAT GAA GAG CAG CAT CTT GAA TCT CAT ACA GAC TGC ATT CTT GCA    1677
     Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys Ile Leu Ala
             470                 475                 480
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GTA AAG CAG GCA ATA TCT GGA ACT TCT CCA GTG GCT TCT TCA TTT CAG    1725
Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser Ser Phe Gln
    485                 490                 495

GGT ATC AAA AAG TCT ATA TTC AGA ATA AGA GAA TCA CCT AAA GAG ACT    1773
Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro Lys Glu Thr
500                 505                 510                 515

TTC AAT GCA AGT TTT TCA GGT CAT ATG ACT GAT CCA AAC TTT AAA AAA    1821
Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn Phe Lys Lys
                520                 525                 530

GAA ACT GAA GCC TCT GAA AGT GGA CTG GAA ATA CAT ACT GTT TGC TCA    1869
Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr Val Cys Ser
            535                 540                 545

CAG AAG GAG GAC TCC TTA TGT CCA AAT TTA ATT GAT AAT GGA AGC TGG    1917
Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn Gly Ser Trp
        550                 555                 560

CCA GCC ACC ACC ACA CAG AAT TCT GTA GCT TTG AAG AAT GCA GGT TTA    1965
Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn Ala Gly Leu
    565                 570                 575

ATA TCC ACT TTG AAA AAG AAA ACA AAT AAG TTT ATT TAT GCT ATA CAT    2013
Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr Ala Ile His
580                 585                 590                 595

GAT GAA ACA TCT TAT AAA GGA AAA AAA ATA CCG AAA GAC CAA AAA TCA    2061
Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp Gln Lys Ser
                600                 605                 610

GAA CTA ATT AAC TGT TCA GCC CAG TTT GAA GCA AAT GCT TTT GAA GCA    2109
Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala Phe Glu Ala
            615                 620                 625

CCA CTT ACA TTT GCA AAT GCT GAT TCA GGT TTA TTG CAT TCT TCT GTG    2157
Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His Ser Ser Val
        630                 635                 640

AAA AGA AGC TGT TCA CAG AAT GAT TCT GAA GAA CCA ACT TTG TCC TTA    2205
Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr Leu Ser Leu
    645                 650                 655

ACT AGC TCT TTT GGG ACA ATT CTG AGG AAA TGT TCT AGA AAT GAA ACA    2253
Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg Asn Glu Thr
660                 665                 670                 675

TGT TCT AAT AAT ACA GTA ATC TCT CAG GAT CTT GAT TAT AAA GAA GCA    2301
Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr Lys Glu Ala
                680                 685                 690

AAA TGT AAT AAG GAA AAA CTA CAG TTA TTT ATT ACC CCA GAA GCT GAT    2349
Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro Glu Ala Asp
            695                 700                 705

TCT CTG TCA TGC CTG CAG GAA GGA CAG TGT GAA AAT GAT CCA AAA AGC    2397
Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp Pro Lys Ser
        710                 715                 720
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AAA AAA GTT TCA GAT ATA AAA GAA GAG GTC TTG GCT GCA GCA TGT CAC    2445
Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala Ala Cys His
    725                 730                 735

CCA GTA CAA CAT TCA AAA GTG GAA TAC AGT GAT ACT GAC TTT CAA TCC    2493
Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp Phe Gln Ser
740                 745                 750                 755

CAG AAA AGT CTT TTA TAT GAT CAT GAA AAT GCC AGC ACT CTT ATT TTA    2541
Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr Leu Ile Leu
                760                 765                 770

ACT CCT ACT TCC AAG GAT GTT CTG TCA AAC CTA GTC ATG ATT TCT AGA    2589
Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met Ile Ser Arg
            775                 780                 785

GGC AAA GAA TCA TAC AAA ATG TCA GAC AAG CTC AAA GGT AAC AAT TAT    2637
Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly Asn Asn Tyr
        790                 795                 800

GAA TCT GAT GTT GAA TTA ACC AAA AAT ATT CCC ATG GAA AAG AAT CAA    2685
Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu Lys Asn Gln
    805                 810                 815

GAT GTA TGT GCT TTA AAT GAA AAT TAT AAA AAC GTT GAG CTG TTG CCA    2733
Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu Leu Leu Pro
820                 825                 830                 835

CCT GAA AAA TAC ATG AGA GTA GCA TCA CCT TCA AGA AAG GTA CAA TTC    2781
Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys Val Gln Phe
                840                 845                 850

AAC CAA AAC ACA AAT CTA AGA GTA ATC CAA AAA AAT CAA GAA GAA ACT    2829
Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln Glu Glu Thr
            855                 860                 865

ACT TCA ATT TCA AAA ATA ACT GTC AAT CCA GAC TCT GAA GAA CTT TTC    2877
Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu Glu Leu Phe
        870                 875                 880

TCA GAC AAT GAG AAT AAT TTT GTC TTC CAA GTA GCT AAT GAA AGG AAT    2925
Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn Glu Arg Asn
    885                 890                 895

AAT CTT GCT TTA GGA AAT ACT AAG GAA CTT CAT GAA ACA GAC TTG ACT    2973
Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr Asp Leu Thr
900                 905                 910                 915

TGT GTA AAC GAA CCC ATT TTC AAG AAC TCT ACC ATG GTT TTA TAT GGA    3021
Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val Leu Tyr Gly
                920                 925                 930

GAC ACA GGT GAT AAA CAA GCA ACC CAA GTG TCA ATT AAA AAA GAT TTG    3069
Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys Lys Asp Leu
            935                 940                 945

GTT TAT GTT CTT GCA GAG GAG AAC AAA AAT AGT GTA AAG CAG CAT ATA    3117
Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys Gln His Ile
        950                 955                 960

AAA ATG ACT CTA GGT CAA GAT TTA AAA TCG GAC ATC TCC TTG AAT ATA    3165
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Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser Leu Asn Ile
    965                 970                 975

GAT AAA ATA CCA GAA AAA AAT AAT GAT TAC ATG AAC AAA TGG GCA GGA    3213
Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asn Lys Trp Ala Gly
980                 985                 990                 995

CTC TTA GGT CCA ATT TCA AAT CAC AGT TTT GGA GGT AGC TTC AGA ACA    3261
Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser Phe Arg Thr
               1000                1005                1010

GCT TCA AAT AAG GAA ATC AAG CTC TCT GAA CAT AAC ATT AAG AAG AGC    3309
Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile Lys Lys Ser
          1015                1020                1025

AAA ATG TTC TTC AAA GAT ATT GAA GAA CAA TAT CCT ACT AGT TTA GCT    3357
Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr Ser Leu Ala
     1030                1035                1040

TGT GTT GAA ATT GTA AAT ACC TTG GCA TTA GAT AAT CAA AAG AAA CTG    3405
Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln Lys Lys Leu
1045                1050                1055

AGC AAG CCT CAG TCA ATT AAT ACT GTA TCT GCA CAT TTA CAG AGT AGT    3453
Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu Gln Ser Ser
1060                1065                1070                1075

GTA GTT GTT TCT GAT TGT AAA AAT AGT CAT ATA ACC CCT CAG ATG TTA    3501
Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro Gln Met Leu
               1080                1085                1090

TTT TCC AAG CAG GAT TTT AAT TCA AAC CAT AAT TTA ACA CCT AGC CAA    3549
Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr Pro Ser Gln
          1095                1100                1105

AAG GCA GAA ATT ACA GAA CTT TCT ACT ATA TTA GAA GAA TCA GGA AGT    3597
Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu Ser Gly Ser
     1110                1115                1120

CAG TTT GAA TTT ACT CAG TTT AGA AAR CCA AGC TAC ATA TTG CAG AAG    3645
Gln Phe Glu Phe Thr Gln Phe Arg Xaa Pro Ser Tyr Ile Leu Gln Lys
1125                1130                1135

AGT ACA TTT GAA GTG CCT GAA AAC CAG ATG ACT ATC TTA AAG ACC ACT    3693
Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu Lys Thr Thr
1140                1145                1150                1155

TCT GAG GAA TGC AGA GAT GCT GAT CTT CAT GTC ATA ATG AAT GCC CCA    3741
Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met Asn Ala Pro
               1160                1165                1170

TCG ATT GGT CAG GTA GAC AGC AGC AAG CAA TTT GAA GGT ACA GTT GAA    3789
Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly Thr Val Glu
          1175                1180                1185

ATT AAA CGG AAG TTT GCT GGC CTG TTG AAA AAT GAC TGT AAC AAA AGT    3837
Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys Asn Lys Ser
     1190                1195                1200

GCT TCT GGT TAT TTA ACA GAT GAA AAT GAA GTG GGG TTT AGG GGC TTT    3885
Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe Arg Gly Phe
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      1205                1210                1215

    TAT TCT GCT CAT GGC ACA AAA CTG AAT GTT TCT ACT GAA GCT CTG CAA    3933
    Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu Ala Leu Gln
1220                1225                1230                1235

    AAA GCT GTG AAA CTG TTT AGT GAT ATT GAG AAT ATT AGT GAG GAA ACT    3981
    Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser Glu Glu Thr
                1240                1245                1250

    TCT GCA GAG GTA CAT CCA ATA AGT TTA TCT TCA AGT AAA TGT CAT GAT    4029
    Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys Cys His Asp
           1255                1260                1265

    TCT GTC GTT TCA ATG TTT AAG ATA GAA AAT CAT AAT GAT AAA ACT GTA    4077
    Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp Lys Thr Val
      1270                1275                1280

    AGT GAA AAA AAT AAT AAA TGC CAA CTG ATA TTA CAA AAT AAT ATT GAA    4125
    Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn Asn Ile Glu
   1285                1290                1295

    ATG ACT ACT GGC ACT TTT GTT GAA GAA ATT ACT GAA AAT TAC AAG AGA    4173
    Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn Tyr Lys Arg
1300                1305                1310                1315

    AAT ACT GAA AAT GAA GAT AAC AAA TAT ACT GCT GCC AGT AGA AAT TCT    4221
    Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser Arg Asn Ser
                1320                1325                1330

    CAT AAC TTA GAA TTT GAT GGC AGT GAT TCA AGT AAA AAT GAT ACT GTT    4269
    His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn Asp Thr Val
           1335                1340                1345

    TGT ATT CAT AAA GAT GAA ACG GAC TTG CTA TTT ACT GAT CAG CAC AAC    4317
    Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp Gln His Asn
      1350                1355                1360

    ATA TGT CTT AAA TTA TCT GGC CAG TTT ATG AAG GAG GGA AAC ACT CAG    4365
    Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly Asn Thr Gln
   1365                1370                1375

    ATT AAA GAA GAT TTG TCA GAT TTA ACT TTT TTG GAA GTT GCG AAA GCT    4413
    Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val Ala Lys Ala
1380                1385                1390                1395

    CAA GAA GCA TGT CAT GGT AAT ACT TCA AAT AAA GAA CAG TTA ACT GCT    4461
    Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln Leu Thr Ala
                1400                1405                1410

    ACT AAA ACG GAG CAA AAT ATA AAA GAT TTT GAG ACT TCT GAT ACA TTT    4509
    Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser Asp Thr Phe
           1415                1420                1425

    TTT CAG ACT GCA AGT GGG AAA AAT ATT AGT GTC GCC AAA GAG TCA TTT    4557
    Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys Glu Ser Phe
      1430                1435                1440

    AAT AAA ATT GTA AAT TTC TTT GAT CAG AAA CCA GAA GAA TTG CAT AAC    4605
    Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu Leu His Asn
   1445                1450                1455
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      TTT TCC TTA AAT TCT GAA TTA CAT TCT GAC ATA AGA AAG AAC AAA ATG    4653
      Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys Asn Lys Met
 5  1460                1465                1470                1475

      GAC ATT CTA AGT TAT GAG GAA ACA GAC ATA GTT AAA CAC AAA ATA CTG    4701
      Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His Lys Ile Leu
                     1480                1485                1490
10
      AAA GAA AGT GTC CCA GTT GGT ACT GGA AAT CAA CTA GTG ACC TTC CAG    4749
      Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val Thr Phe Gln
                1495                1500                1505

15    GGA CAA CCC GAA CGT GAT GAA AAG ATC AAA GAA CCT ACT CTG TTG GGT    4797
      Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr Leu Leu Gly
           1510                1515                1520

      TTT CAT ACA GCT AGC GGG AAA AAA GTT AAA ATT GCA AAG GAA TCT TTG    4845
20    Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys Glu Ser Leu
         1525                1530                1535

      GAC AAA GTG AAA AAC CTT TTT GAT GAA AAA GAG CAA GGT ACT AGT GAA    4893
      Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly Thr Ser Glu
25  1540                1545                1550                1555

      ATC ACC AGT TTT AGC CAT CAA TGG GCA AAG ACC CTA AAG TAC AGA GAG    4941
      Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys Tyr Arg Glu
                     1560                1565                1570
30
      GCC TGT AAA GAC CTT GAA TTA GCA TGT GAG ACC ATT GAG ATC ACA GCT    4989
      Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu Ile Thr Ala
                1575                1580                1585

35    GCC CCA AAG TGT AAA GAA ATG CAG AAT TCT CTC AAT AAT GAT AAA AAC    5037
      Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn Asp Lys Asn
           1590                1595                1600

      CTT GTT TCT ATT GAG ACT GTG GTG CCA CCT AAG CTC TTA AGT GAT AAT    5085
40    Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu Ser Asp Asn
         1605                1610                1615

      TTA TGT AGA CAA ACT GAA AAT CTC AAA ACA TCA AAA AGT ATC TTT TTG    5133
      Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser Ile Phe Leu
45  1620                1625                1630                1635

      AAA GTT AAA GTA CAT GAA AAT GTA GAA AAA GAA ACA GCA AAA AGT CCT    5181
      Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala Lys Ser Pro
                     1640                1645                1650
50
      GCA ACT TGT TAC ACA AAT CAG TCC CCT TAT TCA GTC ATT GAA AAT TCA    5229
      Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile Glu Asn Ser
                1655                1660                1665

55    GCC TTA GCT TTT TAC ACA AGT TGT AGT AGA AAA ACT TCT GTG AGT CAG    5277
      Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser Val Ser Gln
           1670                1675                1680

      ACT TCA TTA CTT GAA GCA AAA AAA TGG CTT AGA GAA GGA ATA TTT GAT    5325
60    Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly Ile Phe Asp
         1685                1690                1695
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GGT CAA CCA GAA AGA ATA AAT ACT GCA GAT TAT GTA GGA AAT TAT TTG 5373
Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly Asn Tyr Leu
1700 1705 1710 1715

TAT GAA AAT AAT TCA AAC AGT ACT ATA GCT GAA AAT GAC AAA AAT CAT 5421
Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp Lys Asn His
1720 1725 1730

CTC TCC GAA AAA CAA GAT ACT TAT TTA AGT AAC AGT AGC ATG TCT AAC 5469
Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser Met Ser Asn
1735 1740 1745

AGC TAT TCC TAC CAT TCT GAT GAG GTA TAT AAT GAT TCA GGA TAT CTC 5517
Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser Gly Tyr Leu
1750 1755 1760

TCA AAA AAT AAA CTT GAT TCT GGT ATT GAG CCA GTA TTG AAG AAT GTT 5565
Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu Lys Asn Val
1765 1770 1775

GAA GAT CAA AAA AAC ACT AGT TTT TCC AAA GTA ATA TCC AAT GTA AAA 5613
Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser Asn Val Lys
1780 1785 1790 1795

GAT GCA AAT GCA TAC CCA CAA ACT GTA AAT GAA GAT ATT TGC GTT GAG 5661
Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile Cys Val Glu
1800 1805 1810

GAA CTT GTG ACT AGC TCT TCA CCC TGC AAA AAT AAA AAT GCA GCC ATT 5709
Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn Ala Ala Ile
1815 1820 1825

AAA TTG TCC ATA TCT AAT AGT AAT AAT TTT GAG GTA GGG CCA CCT GCA 5757
Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly Pro Pro Ala
1830 1835 1840

TTT AGG ATA GCC AGT GGT AAA ATC GTT TGT GTT TCA CAT GAA ACA ATT 5805
Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His Glu Thr Ile
1845 1850 1855

AAA AAA GTG AAA GAC ATA TTT ACA GAC AGT TTC AGT AAA GTA ATT AAG 5853
Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys Val Ile Lys
1860 1865 1870 1875

GAA AAC AAC GAG AAT AAA TCA AAA ATT TGC CAA ACG AAA ATT ATG GCA 5901
Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys Ile Met Ala
1880 1885 1890

GGT TGT TAC GAG GCA TTG GAT GAT TCA GAG GAT ATT CTT CAT AAC TCT 5949
Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu His Asn Ser
1895 1900 1905

CTA GAT AAT GAT GAA TGT AGC ACG CAT TCA CAT AAG GTT TTT GCT GAC 5997
Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val Phe Ala Asp
1910 1915 1920

ATT CAG AGT GAA GAA ATT TTA CAA CAT AAC CAA AAT ATG TCT GGA TTG 6045
Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met Ser Gly Leu
1925 1930 1935

GAG AAA GTT TCT AAA ATA TCA CCT TGT GAT GTT AGT TTG GAA ACT TCA 6093

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Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu Glu Thr Ser
1940                1945                1950                1955

GAT ATA TGT AAA TGT AGT ATA GGG AAG CTT CAT AAG TCA GTC TCA TCT     6141
Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser Val Ser Ser
                1960                1965                1970

GCA AAT ACT TGT GGG ATT TTT AGC ACA GCA AGT GGA AAA TCT GTC CAG     6189
Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys Ser Val Gln
            1975                1980                1985

GTA TCA GAT GCT TCA TTA CAA AAC GCA AGA CAA GTG TTT TCT GAA ATA     6237
Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe Ser Glu Ile
        1990                1995                2000

GAA GAT AGT ACC AAG CAA GTC TTT TCC AAA GTA TTG TTT AAA AGT AAC     6285
Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe Lys Ser Asn
    2005                2010                2015

GAA CAT TCA GAC CAG CTC ACA AGA GAA GAA AAT ACT GCT ATA CGT ACT     6333
Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala Ile Arg Thr
2020                2025                2030                2035

CCA GAA CAT TTA ATA TCC CAA AAA GGC TTT TCA TAT AAT GTG GTA AAT     6381
Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn Val Val Asn
                2040                2045                2050

TCA TCT GCT TTC TCT GGA TTT AGT ACA GCA AGT GGA AAG CAA GTT TCC     6429
Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys Gln Val Ser
            2055                2060                2065

ATT TTA GAA AGT TCC TTA CAC AAA GTT AAG GGA GTG TTA GAG GAA TTT     6477
Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu Glu Glu Phe
        2070                2075                2080

GAT TTA ATC AGA ACT GAG CAT AGT CTT CAC TAT TCA CCT ACG TCT AGA     6525
Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro Thr Ser Arg
    2085                2090                2095

CAA AAT GTA TCA AAA ATA CTT CCT CGT GTT GAT AAG AGA AAC CCA GAG     6573
Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg Asn Pro Glu
2100                2105                2110                2115

CAC TGT GTA AAC TCA GAA ATG GAA AAA ACC TGC AGT AAA GAA TTT AAA     6621
His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys Glu Phe Lys
                2120                2125                2130

TTA TCA AAT AAC TTA AAT GTT GAA GGT GGT TCT TCA GAA AAT AAT CAC     6669
Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu Asn Asn His
            2135                2140                2145

TCT ATT AAA GTT TCT CCA TAT CTC TCT CAA TTT CAA CAA GAC AAA CAA     6717
Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln Asp Lys Gln
        2150                2155                2160

CAG TTG GTA TTA GGA ACC AAA GTC TCA CTT GTT GAG AAC ATT CAT GTT     6765
Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn Ile His Val
    2165                2170                2175

TTG GGA AAA GAA CAG GCT TCA CCT AAA AAC GTA AAA ATG GAA ATT GGT     6813
Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met Glu Ile Gly
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2180                2185                2190                2195

 AAA ACT GAA ACT TTT TCT GAT GTT CCT GTG AAA ACA AAT ATA GAA GTT    6861
 Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn Ile Glu Val
                  2200                2205                2210

 TGT TCT ACT TAC TCC AAA GAT TCA GAA AAC TAC TTT GAA ACA GAA GCA    6909
 Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu Thr Glu Ala
             2215                2220                2225

 GTA GAA ATT GCT AAA GCT TTT ATG GAA GAT GAT GAA CTG ACA GAT TCT    6957
 Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu Thr Asp Ser
         2230                2235                2240

 AAA CTG CCA AGT CAT GCC ACA CAT TCT CTT TTT ACA TGT CCC GAA AAT    7005
 Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys Pro Glu Asn
    2245                2250                2255

 GAG GAA ATG GTT TTG TCA AAT TCA AGA ATT GGA AAA AGA AGA GGA GAG    7053
 Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg Arg Gly Glu
2260                2265                2270                2275

 CCC CTT ATC TTA GTG GGA GAA CCC TCA ATC AAA AGA AAC TTA TTA AAT    7101
 Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn Leu Leu Asn
                  2280                2285                2290

 GAA TTT GAC AGG ATA ATA GAA AAT CAA GAA AAA TCC TTA AAG GCT TCA    7149
 Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu Lys Ala Ser
             2295                2300                2305

 AAA AGC ACT CCA GAT GGC ACA ATA AAA GAT CGA AGA TTG TTT ATG CAT    7197
 Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu Phe Met His
         2310                2315                2320

 CAT GTT TCT TTA GAG CCG ATT ACC TGT GTA CCC TTT CGC ACA ACT AAG    7245
 His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg Thr Thr Lys
    2325                2330                2335

 GAA CGT CAA GAG ATA CAG AAT CCA AAT TTT ACC GCA CCT GGT CAA GAA    7293
 Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro Gly Gln Glu
2340                2345                2350                2355

 TTT CTG TCT AAA TCT CAT TTG TAT GAA CAT CTG ACT TTG GAA AAA TCT    7341
 Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu Glu Lys Ser
                  2360                2365                2370

 TCA AGC AAT TTA GCA GTT TCA GGA CAT CCA TTT TAT CAA GTT TCT GCT    7389
 Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln Val Ser Ala
             2375                2380                2385

 ACA AGA AAT GAA AAA ATG AGA CAC TTG ATT ACT ACA GGC AGA CCA ACC    7437
 Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly Arg Pro Thr
         2390                2395                2400

 AAA GTC TTT GTT CCA CCT TTT AAA ACT AAA TCA CAT TTT CAC AGA GTT    7485
 Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe His Arg Val
    2405                2410                2415

 GAA CAG TGT GTT AGG AAT ATT AAC TTG GAG GAA AAC AGA CAA AAG CAA    7533
 Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg Gln Lys Gln
2420                2425                2430                2435
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AAC ATT GAT GGA CAT GGC TCT GAT GAT AGT AAA AAT AAG ATT AAT GAC    7581
Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys Ile Asn Asp
                2440                2445                2450

AAT GAG ATT CAT CAG TTT AAC AAA AAC AAC TCC AAT CAA GCA GCA GCT    7629
Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln Ala Ala Ala
            2455                2460                2465

GTA ACT TTC ACA AAG TGT GAA GAA GAA CCT TTA GAT TTA ATT ACA AGT    7677
Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu Ile Thr Ser
        2470                2475                2480

CTT CAG AAT GCC AGA GAT ATA CAG GAT ATG CGA ATT AAG AAG AAA CAA    7725
Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys Lys Lys Gln
    2485                2490                2495

AGG CAA CGC GTC TTT CCA CAG CCA GGC AGT CTG TAT CTT GCA AAA ACA    7773
Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu Ala Lys Thr
2500                2505                2510                2515

TCC ACT CTG CCT CGA ATC TCT CTG AAA GCA GCA GTA GGA GGC CAA GTT    7821
Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly Gly Gln Val
                2520                2525                2530

CCC TCT GCG TGT TCT CAT AAA CAG CTG TAT ACG TAT GGC GTT TCT AAA    7869
Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly Val Ser Lys
            2535                2540                2545

CAT TGC ATA AAA ATT AAC AGC AAA AAT GCA GAG TCT TTT CAG TTT CAC    7917
His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe Gln Phe His
        2550                2555                2560

ACT GAA GAT TAT TTT GGT AAG GAA AGT TTA TGG ACT GGA AAA GGA ATA    7965
Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly Lys Gly Ile
    2565                2570                2575

CAG TTG GCT GAT GGT GGA TGG CTC ATA CCC TCC AAT GAT GGA AAG GCT    8013
Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp Gly Lys Ala
2580                2585                2590                2595

GGA AAA GAA GAA TTT TAT AGG GCT CTG TGT GAC ACT CCA GGT GTG GAT    8061
Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro Gly Val Asp
                2600                2605                2610

CCA AAG CTT ATT TCT AGA ATT TGG GTT TAT AAT CAC TAT AGA TGG ATC    8109
Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr Arg Trp Ile
            2615                2620                2625

ATA TGG AAA CTG GCA GCT ATG GAA TGT GCC TTT CCT AAG GAA TTT GCT    8157
Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys Glu Phe Ala
        2630                2635                2640

AAT AGA TGC CTA AGC CCA GAA AGG GTG CTT CTT CAA CTA AAA TAC AGA    8205
Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu Lys Tyr Arg
    2645                2650                2655

TAT GAT ACG GAA ATT GAT AGA AGC AGA AGA TCG GCT ATA AAA AAG ATA    8253
Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile Lys Lys Ile
2660                2665                2670                2675
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ATG GAA AGG GAT GAC ACA GCT GCA AAA ACA CTT GTT CTC TGT GTT TCT    8301
Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu Cys Val Ser
                2680                2685                2690

GAC ATA ATT TCA TTG AGC GCA AAT ATA TCT GAA ACT TCT AGC AAT AAA    8349
Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser Ser Asn Lys
            2695                2700                2705

ACT AGT AGT GCA GAT ACC CAA AAA GTG GCC ATT ATT GAA CTT ACA GAT    8397
Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu Leu Thr Asp
        2710                2715                2720

GGG TGG TAT GCT GTT AAG GCC CAG TTA GAT CCT CCC CTC TTA GCT GTC    8445
Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu Leu Ala Val
    2725                2730                2735

TTA AAG AAT GGC AGA CTG ACA GTT GGT CAG AAG ATT ATT CTT CAT GGA    8493
Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile Leu His Gly
2740                2745                2750                2755

GCA GAA CTG GTG GGC TCT CCT GAT GCC TGT ACA CCT CTT GAA GCC CCA    8541
Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu Glu Ala Pro
                2760                2765                2770

GAA TCT CTT ATG TTA AAG ATT TCT GCT AAC AGT ACT CGG CCT GCT CGC    8589
Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg Pro Ala Arg
            2775                2780                2785

TGG TAT ACC AAA CTT GGA TTC TTT CCT GAC CCT AGA CCT TTT CCT CTG    8637
Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro Phe Pro Leu
        2790                2795                2800

CCC TTA TCA TCG CTT TTC AGT GAT GGA GGA AAT GTT GGT TGT GTT GAT    8685
Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly Cys Val Asp
    2805                2810                2815

GTA ATT ATT CAA AGA GCA TAC CCT ATA CAG TGG ATG GAG AAG ACA TCA    8733
Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu Lys Thr Ser
2820                2825                2830                2835

TCT GGA TTA TAC ATA TTT CGC AAT GAA AGA GAG GAA GAA AAG GAA GCA    8781
Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu Lys Glu Ala
                2840                2845                2850

GCA AAA TAT GTG GAG GCC CAA CAA AAG AGA CTA GAA GCC TTA TTC ACT    8829
Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala Leu Phe Thr
            2855                2860                2865

AAA ATT CAG GAG GAA TTT GAA GAA CAT GAA GAA AAC ACA ACA AAA CCA    8877
Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr Thr Lys Pro
        2870                2875                2880

TAT TTA CCA TCA CGT GCA CTA ACA AGA CAG CAA GTT CGT GCT TTG CAA    8925
Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg Ala Leu Gln
    2885                2890                2895

GAT GGT GCA GAG CTT TAT GAA GCA GTG AAG AAT GCA GCA GAC CCA GCT    8973
Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala Asp Pro Ala
2900                2905                2910                2915

TAC CTT GAG GGT TAT TTC AGT GAA GAG CAG TTA AGA GCC TTG AAT AAT    9021
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      Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala Leu Asn Asn
                     2920                2925                2930

 5    CAC AGG CAA ATG TTG AAT GAT AAG AAA CAA GCT CAG ATC CAG TTG GAA    9069
      His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile Gln Leu Glu
                2935                2940                2945

      ATT AGG AAG GCC ATG GAA TCT GCT GAA CAA AAG GAA CAA GGT TTA TCA    9117
10    Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln Gly Leu Ser
           2950                2955                2960

      AGG GAT GTC ACA ACC GTG TGG AAG TTG CGT ATT GTA AGC TAT TCA AAA    9165
      Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser Tyr Ser Lys
15       2965                2970                2975

      AAA GAA AAA GAT TCA GTT ATA CTG AGT ATT TGG CGT CCA TCA TCA GAT    9213
      Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro Ser Ser Asp
     2980                2985                2990                2995
20
      TTA TAT TCT CTG TTA ACA GAA GGA AAG AGA TAC AGA ATT TAT CAT CTT    9261
      Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile Tyr His Leu
                     3000                3005                3010

25    GCA ACT TCA AAA TCT AAA AGT AAA TCT GAA AGA GCT AAC ATA CAG TTA    9309
      Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn Ile Gln Leu
                3015                3020                3025

      GCA GCG ACA AAA AAA ACT CAG TAT CAA CAA CTA CCG GTT TCA GAT GAA    9357
30    Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val Ser Asp Glu
           3030                3035                3040

      ATT TTA TTT CAG ATT TAC CAG CCA CGG GAG CCC CTT CAC TTC AGC AAA    9405
      Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His Phe Ser Lys
35       3045                3050                3055

      TTT TTA GAT CCA GAC TTT CAG CCA TCT TGT TCT GAG GTG GAC CTA ATA    9453
      Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val Asp Leu Ile
     3060                3065                3070                3075
40
      GGA TTT GTC GTT TCT GTT GTG AAA AAA ACA GGA CTT GCC CCT TTC GTC    9501
      Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala Pro Phe Val
                     3080                3085                3090

45    TAT TTG TCA GAC GAA TGT TAC AAT TTA CTG GCA ATA AAG TTT TGG ATA    9549
      Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys Phe Trp Ile
                3095                3100                3105

      GAC CTT AAT GAG GAC ATT ATT AAG CCT CAT ATG TTA ATT GCT GCA AGC    9597
50    Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile Ala Ala Ser
           3110                3115                3120

      AAC CTC CAG TGG CGA CCA GAA TCC AAA TCA GGC CTT CTT ACT TTA TTT    9645
      Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu Thr Leu Phe
55       3125                3130                3135

      GCT GGA GAT TTT TCT GTG TTT TCT GCT AGT CCA AAA GAG GGC CAC TTT    9693
      Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu Gly His Phe
     3140                3145                3150                3155
60
      CAA GAG ACA TTC AAC AAA ATG AAA AAT ACT GTT GAG AAT ATT GAC ATA    9741
      Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn Ile Asp Ile
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                    3160                3165                3170

     CTT TGC AAT GAA GCA GAA AAC AAG CTT ATG CAT ATA CTG CAT GCA AAT    9789
 5   Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu His Ala Asn
               3175                3180                3185

     GAT CCC AAG TGG TCC ACC CCA ACT AAA GAC TGT ACT TCA GGG CCG TAC    9837
     Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser Gly Pro Tyr
10          3190                3195                3200

     ACT GCT CAA ATC ATT CCT GGT ACA GGA AAC AAG CTT CTG ATG TCT TCT    9885
     Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu Met Ser Ser
        3205                3210                3215
15
     CCT AAT TGT GAG ATA TAT TAT CAA AGT CCT TTA TCA CTT TGT ATG GCC    9933
     Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu Cys Met Ala
    3220                3225                3230                3235

20   AAA AGG AAG TCT GTT TCC ACA CCT GTC TCA GCC CAG ATG ACT TCA AAG    9981
     Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met Thr Ser Lys
                    3240                3245                3250

     TCT TGT AAA GGG GAG AAA GAG ATT GAT GAC CAA AAG AAC TGC AAA AAG   10029
25   Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn Cys Lys Lys
               3255                3260                3265

     AGA AGA GCC TTG GAT TTC TTG AGT AGA CTG CCT TTA CCT CCA CCT GTT   10077
     Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro Pro Pro Val
30          3270                3275                3280

     AGT CCC ATT TGT ACA TTT GTT TCT CCG GCT GCA CAG AAG GCA TTT CAG   10125
     Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys Ala Phe Gln
        3285                3290                3295
35
     CCA CCA AGG AGT TGT GGC ACC AAA TAC GAA ACA CCC ATA AAG AAA AAA   10173
     Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile Lys Lys Lys
    3300                3305                3310                3315

40   GAA CTG AAT TCT CCT CAG ATG ACT CCA TTT AAA AAA TTC AAT GAA ATT   10221
     Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe Asn Glu Ile
                    3320                3325                3330

     TCT CTT TTG GAA AGT AAT TCA ATA GCT GAC GAA GAA CTT GCA TTG ATA   10269
45   Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile
               3335                3340                3345

     AAT ACC CAA GCT CTT TTG TCT GGT TCA ACA GGA GAA AAA CAA TTT ATA   10317
     Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys Gln Phe Ile
50          3350                3355                3360

     TCT GTC AGT GAA TCC ACT AGG ACT GCT CCC ACC AGT TCA GAA GAT TAT   10365
     Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp Tyr
        3365                3370                3375
55
     CTC AGA CTG AAA CGA CGT TGT ACT ACA TCT CTG ATC AAA GAA CAG GAG   10413
     Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu Gln Glu
    3380                3385                3390                3395

60   AGT TCC CAG GCC AGT ACG GAA GAA TGT GAG AAA AAT AAG CAG GAC ACA   10461
     Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys Gln Asp Thr
                    3400                3405                3410
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ATT ACA ACT AAA AAA TAT ATC TAA                                          10485
Ile Thr Thr Lys Lys Tyr Ile
          3415
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(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3418 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

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Met Pro Ile Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys
 1               5                  10                  15
Thr Arg Cys Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe
            20                  25                  30
Glu Glu Leu Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu
        35                  40                  45
Glu Ser Glu His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr
    50                  55                  60
Pro Gln Arg Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile
65                  70                  75                  80
Phe Lys Glu Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys
                85                  90                  95
Glu Leu Asp Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser
            100                 105                 110
Arg His Lys Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp
        115                 120                 125
Asp Val Ser Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val
    130                 135                 140
Val Leu Gln Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val
145                 150                 155                 160
Cys Gly Ser Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr
                165                 170                 175
Pro Lys His Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met
            180                 185                 190
Ser Trp Ser Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val
        195                 200                 205
Leu Ile Val Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp
    210                 215                 220
Thr Thr Ala Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu
225                 230                 235                 240
Lys Lys Asn Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr
                245                 250                 255
Asn Gln Arg Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn
            260                 265                 270
Ser Phe Lys Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro
        275                 280                 285
Asn Val Leu Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu
    290                 295                 300
Glu Asp Ser Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu
305                 310                 315                 320
Gln Lys Val Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala
                325                 330                 335
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Asn Ala Asp Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr
            340                 345                 350
Ser Phe Val Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser
        355                 360                 365
Asn Val Ala His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser
    370                 375                 380
Lys Glu Val Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu
385                 390                 395                 400
Ser Gly Leu Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile
                405                 410                 415
Ser Ser Cys Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu
            420                 425                 430
Asn Lys Arg Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg
        435                 440                 445
Ile Ser Ser Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val
    450                 455                 460
Val Asn Lys Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys
465                 470                 475                 480
Ile Leu Ala Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser
                485                 490                 495
Ser Phe Gln Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro
            500                 505                 510
Lys Glu Thr Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn
        515                 520                 525
Phe Lys Lys Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr
    530                 535                 540
Val Cys Ser Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn
545                 550                 555                 560
Gly Ser Trp Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn
                565                 570                 575
Ala Gly Leu Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr
            580                 585                 590
Ala Ile His Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp
        595                 600                 605
Gln Lys Ser Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala
    610                 615                 620
Phe Glu Ala Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His
625                 630                 635                 640
Ser Ser Val Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr
                645                 650                 655
Leu Ser Leu Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg
            660                 665                 670
Asn Glu Thr Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr
        675                 680                 685
Lys Glu Ala Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro
    690                 695                 700
Glu Ala Asp Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp
705                 710                 715                 720
Pro Lys Ser Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala
                725                 730                 735
Ala Cys His Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp
            740                 745                 750
Phe Gln Ser Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr
        755                 760                 765
Leu Ile Leu Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met
    770                 775                 780
Ile Ser Arg Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly
785                 790                 795                 800
Asn Asn Tyr Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu
                805                 810                 815
Lys Asn Gln Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu
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820 825 830
Leu Leu Pro Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys
835 840 845
Val Gln Phe Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln
850 855 860
Glu Glu Thr Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu
865 870 875 880
Glu Leu Phe Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn
885 890 895
Glu Arg Asn Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr
900 905 910
Asp Leu Thr Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val
915 920 925
Leu Tyr Gly Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys
930 935 940
Lys Asp Leu Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys
945 950 955 960
Gln His Ile Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser
965 970 975
Leu Asn Ile Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asn Lys
980 985 990
Trp Ala Gly Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser
995 1000 1005
Phe Arg Thr Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile
1010 1015 1020
Lys Lys Ser Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr
1025 1030 1035 104
Ser Leu Ala Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln
1045 1050 1055
Lys Lys Leu Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu
1060 1065 1070
Gln Ser Ser Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro
1075 1080 1085
Gln Met Leu Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr
1090 1095 1100
Pro Ser Gln Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu
1105 1110 1115 112
Ser Gly Ser Gln Phe Glu Phe Thr Gln Phe Arg Xaa Pro Ser Tyr Ile
1125 1130 1135
Leu Gln Lys Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu
1140 1145 1150
Lys Thr Thr Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met
1155 1160 1165
Asn Ala Pro Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly
1170 1175 1180
Thr Val Glu Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys
1185 1190 1195 120
Asn Lys Ser Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe
1205 1210 1215
Arg Gly Phe Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu
1220 1225 1230
Ala Leu Gln Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser
1235 1240 1245
Glu Glu Thr Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys
1250 1255 1260
Cys His Asp Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp
1265 1270 1275 128
Lys Thr Val Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn
1285 1290 1295
Asn Ile Glu Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn
1300 1305 1310

Tyr Lys Arg Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser
1315 1320 1325
Arg Asn Ser His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn
1330 1335 1340
Asp Thr Val Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp
1345 1350 1355 136
Gln His Asn Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly
1365 1370 1375
Asn Thr Gln Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val
1380 1385 1390
Ala Lys Ala Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln
1395 1400 1405
Leu Thr Ala Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser
1410 1415 1420
Asp Thr Phe Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys
1425 1430 1435 144
Glu Ser Phe Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu
1445 1450 1455
Leu His Asn Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys
1460 1465 1470
Asn Lys Met Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His
1475 1480 1485
Lys Ile Leu Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val
1490 1495 1500
Thr Phe Gln Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr
1505 1510 1515 152
Leu Leu Gly Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys
1525 1530 1535
Glu Ser Leu Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly
1540 1545 1550
Thr Ser Glu Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys
1555 1560 1565
Tyr Arg Glu Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu
1570 1575 1580
Ile Thr Ala Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn
1585 1590 1595 160
Asp Lys Asn Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu
1605 1610 1615
Ser Asp Asn Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser
1620 1625 1630
Ile Phe Leu Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala
1635 1640 1645
Lys Ser Pro Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile
1650 1655 1660
Glu Asn Ser Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser
1665 1670 1675 168
Val Ser Gln Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly
1685 1690 1695
Ile Phe Asp Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly
1700 1705 1710
Asn Tyr Leu Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp
1715 1720 1725
Lys Asn His Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser
1730 1735 1740
Met Ser Asn Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser
1745 1750 1755 176
Gly Tyr Leu Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu
1765 1770 1775
Lys Asn Val Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser
1780 1785 1790
Asn Val Lys Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile

1795 1800 1805

Cys Val Glu Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn
1810 1815 1820

Ala Ala Ile Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly
1825 1830 1835 184

Pro Pro Ala Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His
1845 1850 1855

Glu Thr Ile Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys
1860 1865 1870

Val Ile Lys Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys
1875 1880 1885

Ile Met Ala Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu
1890 1895 1900

His Asn Ser Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val
1905 1910 1915 192

Phe Ala Asp Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met
1925 1930 1935

Ser Gly Leu Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu
1940 1945 1950

Glu Thr Ser Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser
1955 1960 1965

Val Ser Ser Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys
1970 1975 1980

Ser Val Gln Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe
1985 1990 1995 200

Ser Glu Ile Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe
2005 2010 2015

Lys Ser Asn Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala
2020 2025 2030

Ile Arg Thr Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn
2035 2040 2045

Val Val Asn Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys
2050 2055 2060

Gln Val Ser Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu
2065 2070 2075 208

Glu Glu Phe Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro
2085 2090 2095

Thr Ser Arg Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg
2100 2105 2110

Asn Pro Glu His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys
2115 2120 2125

Glu Phe Lys Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu
2130 2135 2140

Asn Asn His Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln
2145 2150 2155 216

Asp Lys Gln Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn
2165 2170 2175

Ile His Val Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met
2180 2185 2190

Glu Ile Gly Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn
2195 2200 2205

Ile Glu Val Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu
2210 2215 2220

Thr Glu Ala Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu
2225 2230 2235 224

Thr Asp Ser Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys
2245 2250 2255

Pro Glu Asn Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg
2260 2265 2270

Arg Gly Glu Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn
2275 2280 2285

Leu Leu Asn Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu
2290 2295 2300
Lys Ala Ser Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu
2305 2310 2315 232
Phe Met His His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg
2325 2330 2335
Thr Thr Lys Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro
2340 2345 2350
Gly Gln Glu Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu
2355 2360 2365
Glu Lys Ser Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln
2370 2375 2380
Val Ser Ala Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly
2385 2390 2395 240
Arg Pro Thr Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe
2405 2410 2415
His Arg Val Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg
2420 2425 2430
Gln Lys Gln Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys
2435 2440 2445
Ile Asn Asp Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln
2450 2455 2460
Ala Ala Ala Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu
2465 2470 2475 248
Ile Thr Ser Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys
2485 2490 2495
Lys Lys Gln Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu
2500 2505 2510
Ala Lys Thr Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly
2515 2520 2525
Gly Gln Val Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly
2530 2535 2540
Val Ser Lys His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe
2545 2550 2555 256
Gln Phe His Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly
2565 2570 2575
Lys Gly Ile Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp
2580 2585 2590
Gly Lys Ala Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro
2595 2600 2605
Gly Val Asp Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr
2610 2615 2620
Arg Trp Ile Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys
2625 2630 2635 264
Glu Phe Ala Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu
2645 2650 2655
Lys Tyr Arg Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile
2660 2665 2670
Lys Lys Ile Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu
2675 2680 2685
Cys Val Ser Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser
2690 2695 2700
Ser Asn Lys Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu
2705 2710 2715 272
Leu Thr Asp Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu
2725 2730 2735
Leu Ala Val Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile
2740 2745 2750
Leu His Gly Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu
2755 2760 2765
Glu Ala Pro Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg

2770 2775 2780

Pro Ala Arg Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro
2785 2790 2795 280

Phe Pro Leu Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly
2805 2810 2815

Cys Val Asp Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu
2820 2825 2830

Lys Thr Ser Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu
2835 2840 2845

Lys Glu Ala Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala
2850 2855 2860

Leu Phe Thr Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr
2865 2870 2875 288

Thr Lys Pro Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg
2885 2890 2895

Ala Leu Gln Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala
2900 2905 2910

Asp Pro Ala Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala
2915 2920 2925

Leu Asn Asn His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile
2930 2935 2940

Gln Leu Glu Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln
2945 2950 2955 296

Gly Leu Ser Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser
2965 2970 2975

Tyr Ser Lys Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro
2980 2985 2990

Ser Ser Asp Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile
2995 3000 3005

Tyr His Leu Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn
3010 3015 3020

Ile Gln Leu Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val
3025 3030 3035 304

Ser Asp Glu Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His
3045 3050 3055

Phe Ser Lys Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val
3060 3065 3070

Asp Leu Ile Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala
3075 3080 3085

Pro Phe Val Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys
3090 3095 3100

Phe Trp Ile Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile
3105 3110 3115 312

Ala Ala Ser Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu
3125 3130 3135

Thr Leu Phe Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu
3140 3145 3150

Gly His Phe Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn
3155 3160 3165

Ile Asp Ile Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu
3170 3175 3180

His Ala Asn Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser
3185 3190 3195 320

Gly Pro Tyr Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu
3205 3210 3215

Met Ser Ser Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu
3220 3225 3230

Cys Met Ala Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met
3235 3240 3245

Thr Ser Lys Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn
3250 3255 3260

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Cys Lys Lys Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro
3265                3270                3275                328
Pro Pro Val Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys
                    3285                3290                3295
Ala Phe Gln Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile
            3300                3305                3310
Lys Lys Lys Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe
        3315                3320                3325
Asn Glu Ile Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu
    3330                3335                3340
Ala Leu Ile Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys
3345                3350                3355                336
Gln Phe Ile Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser
                    3365                3370                3375
Glu Asp Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys
            3380                3385                3390
Glu Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys
        3395                3400                3405
Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile
    3410                3415
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(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10485 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 229...10482
(D) OTHER INFORMATION: BRCA2 (OMI3)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

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GGTGGCGCGA GCTTCTGAAA CTAGGCGGCA GAGGCGGAGC CGCTGTGGCA CTGCTGCGCC     60
TCTGCTGCGC CTCGGGTGTC TTTTGCGGCG GTGGGTCGCC GCCGGGAGAA GCGTGAGGGG    120
ACAGATTTGT GACCGGCGCG GTTTTTGTCA GCTTACTCCG GCCAAAAAAG AACTGCACCT    180
CTGGAGCGGA CTTATTTACC AAGCATTGGA GGAATATCGT AGGTAAAA ATG CCT ATT    237
                                                        Met Pro Ile
                                                         1

GGA TCC AAA GAG AGG CCA ACA TTT TTT GAA ATT TTT AAG ACA CGC TGC     285
Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys Thr Arg Cys
 5                  10                  15

AAC AAA GCA GAT TTA GGA CCA ATA AGT CTT AAT TGG TTT GAA GAA CTT     333
Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe Glu Glu Leu
20                  25                  30                  35

TCT TCA GAA GCT CCA CCC TAT AAT TCT GAA CCT GCA GAA GAA TCT GAA     381
Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu Glu Ser Glu
                40                  45                  50

CAT AAA AAC AAC AAT TAC GAA CCA AAC CTA TTT AAA ACT CCA CAA AGG     429
His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr Pro Gln Arg
            55                  60                  65
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AAA CCA TCT TAT AAT CAG CTG GCT TCA ACT CCA ATA ATA TTC AAA GAG     477
Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile Phe Lys Glu
        70                  75                  80

CAA GGG CTG ACT CTG CCG CTG TAC CAA TCT CCT GTA AAA GAA TTA GAT     525
Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys Glu Leu Asp
    85                  90                  95

AAA TTC AAA TTA GAC TTA GGA AGG AAT GTT CCC AAT AGT AGA CAT AAA     573
Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser Arg His Lys
100                 105                 110                 115

AGT CTT CGC ACA GTG AAA ACT AAA ATG GAT CAA GCA GAT GAT GTT TCC     621
Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp Asp Val Ser
                120                 125                 130

TGT CCA CTT CTA AAT TCT TGT CTT AGT GAA AGT CCT GTT GTT CTA CAA     669
Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val Val Leu Gln
            135                 140                 145

TGT ACA CAT GTA ACA CCA CAA AGA GAT AAG TCA GTG GTA TGT GGG AGT     717
Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val Cys Gly Ser
        150                 155                 160

TTG TTT CAT ACA CCA AAG TTT GTG AAG GGT CGT CAG ACA CCA AAA CAT     765
Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr Pro Lys His
    165                 170                 175

ATT TCT GAA AGT CTA GGA GCT GAG GTG GAT CCT GAT ATG TCT TGG TCA     813
Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met Ser Trp Ser
180                 185                 190                 195

AGT TCT TTA GCT ACA CCA CCC ACC CTT AGT TCT ACT GTG CTC ATA GTC     861
Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val Leu Ile Val
                200                 205                 210

AGA AAT GAA GAA GCA TCT GAA ACT GTA TTT CCT CAT GAT ACT ACT GCT     909
Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp Thr Thr Ala
            215                 220                 225

AAT GTG AAA AGC TAT TTT TCC AAT CAT GAT GAA AGT CTG AAG AAA AAT     957
Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu Lys Lys Asn
        230                 235                 240

GAT AGA TTT ATC GCT TCT GTG ACA GAC AGT GAA AAC ACA AAT CAA AGA    1005
Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr Asn Gln Arg
    245                 250                 255

GAA GCT GCA AGT CAT GGA TTT GGA AAA ACA TCA GGG AAT TCA TTT AAA    1053
Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn Ser Phe Lys
260                 265                 270                 275

GTA AAT AGC TGC AAA GAC CAC ATT GGA AAG TCA ATG CCA CAT GTC CTA    1101
Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro His Val Leu
                280                 285                 290

GAA GAT GAA GTA TAT GAA ACA GTT GTA GAT ACC TCT GAA GAA GAT AGT    1149
Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu Glu Asp Ser
            295                 300                 305

TTT TCA TTA TGT TTT TCT AAA TGT AGA ACA AAA AAT CTA CAA AAA GTA    1197
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Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu Gln Lys Val
        310                 315                 320

AGA ACT AGC AAG ACT AGG AAA AAA ATT TTC CAT GAA GCA AAC GCT GAT  1245
Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala Asn Ala Asp
    325                 330                 335

GAA TGT GAA AAA TCT AAA AAC CAA GTG AAA GAA AAA TAC TCA TTT GTA  1293
Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr Ser Phe Val
340                 345                 350                 355

TCT GAA GTG GAA CCA AAT GAT ACT GAT CCA TTA GAT TCA AAT GTA GCA  1341
Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser Asn Val Ala
                360                 365                 370

AAT CAG AAG CCC TTT GAG AGT GGA AGT GAC AAA ATC TCC AAG GAA GTT  1389
Asn Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser Lys Glu Val
            375                 380                 385

GTA CCG TCT TTG GCC TGT GAA TGG TCT CAA CTA ACC CTT TCA GGT CTA  1437
Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu Ser Gly Leu
        390                 395                 400

AAT GGA GCC CAG ATG GAG AAA ATA CCC CTA TTG CAT ATT TCT TCA TGT  1485
Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile Ser Ser Cys
    405                 410                 415

GAC CAA AAT ATT TCA GAA AAA GAC CTA TTA GAC ACA GAG AAC AAA AGA  1533
Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu Asn Lys Arg
420                 425                 430                 435

AAG AAA GAT TTT CTT ACT TCA GAG AAT TCT TTG CCA CGT ATT TCT AGC  1581
Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg Ile Ser Ser
                440                 445                 450

CTA CCA AAA TCA GAG AAG CCA TTA AAT GAG GAA ACA GTG GTA AAT AAG  1629
Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val Val Asn Lys
            455                 460                 465

AGA GAT GAA GAG CAG CAT CTT GAA TCT CAT ACA GAC TGC ATT CTT GCA  1677
Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys Ile Leu Ala
        470                 475                 480

GTA AAG CAG GCA ATA TCT GGA ACT TCT CCA GTG GCT TCT TCA TTT CAG  1725
Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser Ser Phe Gln
    485                 490                 495

GGT ATC AAA AAG TCT ATA TTC AGA ATA AGA GAA TCA CCT AAA GAG ACT  1773
Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro Lys Glu Thr
500                 505                 510                 515

TTC AAT GCA AGT TTT TCA GGT CAT ATG ACT GAT CCA AAC TTT AAA AAA  1821
Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn Phe Lys Lys
                520                 525                 530

GAA ACT GAA GCC TCT GAA AGT GGA CTG GAA ATA CAT ACT GTT TGC TCA  1869
Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr Val Cys Ser
            535                 540                 545

CAG AAG GAG GAC TCC TTA TGT CCA AAT TTA ATT GAT AAT GGA AGC TGG  1917
Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn Gly Ser Trp
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                550                 555                 560

     CCA GCC ACC ACC ACA CAG AAT TCT GTA GCT TTG AAG AAT GCA GGT TTA    1965
5    Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn Ala Gly Leu
         565                 570                 575

     ATA TCC ACT TTG AAA AAG AAA ACA AAT AAG TTT ATT TAT GCT ATA CAT    2013
     Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr Ala Ile His
10   580                 585                 590                 595

     GAT GAA ACA TCT TAT AAA GGA AAA AAA ATA CCG AAA GAC CAA AAA TCA    2061
     Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp Gln Lys Ser
                     600                 605                 610
15
     GAA CTA ATT AAC TGT TCA GCC CAG TTT GAA GCA AAT GCT TTT GAA GCA    2109
     Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala Phe Glu Ala
                 615                 620                 625

20   CCA CTT ACA TTT GCA AAT GCT GAT TCA GGT TTA TTG CAT TCT TCT GTG    2157
     Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His Ser Ser Val
             630                 635                 640

     AAA AGA AGC TGT TCA CAG AAT GAT TCT GAA GAA CCA ACT TTG TCC TTA    2205
25   Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr Leu Ser Leu
         645                 650                 655

     ACT AGC TCT TTT GGG ACA ATT CTG AGG AAA TGT TCT AGA AAT GAA ACA    2253
     Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg Asn Glu Thr
30   660                 665                 670                 675

     TGT TCT AAT AAT ACA GTA ATC TCT CAG GAT CTT GAT TAT AAA GAA GCA    2301
     Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr Lys Glu Ala
                     680                 685                 690
35
     AAA TGT AAT AAG GAA AAA CTA CAG TTA TTT ATT ACC CCA GAA GCT GAT    2349
     Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro Glu Ala Asp
                 695                 700                 705

40   TCT CTG TCA TGC CTG CAG GAA GGA CAG TGT GAA AAT GAT CCA AAA AGC    2397
     Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp Pro Lys Ser
             710                 715                 720

     AAA AAA GTT TCA GAT ATA AAA GAA GAG GTC TTG GCT GCA GCA TGT CAC    2445
45   Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala Ala Cys His
         725                 730                 735

     CCA GTA CAA CAC TCA AAA GTG GAA TAC AGT GAT ACT GAC TTT CAA TCC    2493
     Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp Phe Gln Ser
50   740                 745                 750                 755

     CAG AAA AGT CTT TTA TAT GAT CAT GAA AAT GCC AGC ACT CTT ATT TTA    2541
     Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr Leu Ile Leu
                     760                 765                 770
55
     ACT CCT ACT TCC AAG GAT GTT CTG TCA AAC CTA GTC ATG ATT TCT AGA    2589
     Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met Ile Ser Arg
                 775                 780                 785

60   GGC AAA GAA TCA TAC AAA ATG TCA GAC AAG CTC AAA GGT AAC AAT TAT    2637
     Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly Asn Asn Tyr
             790                 795                 800
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GAA TCT GAT GTT GAA TTA ACC AAA AAT ATT CCC ATG GAA AAG AAT CAA    2685
Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu Lys Asn Gln
    805                 810                 815

GAT GTA TGT GCT TTA AAT GAA AAT TAT AAA AAC GTT GAG CTG TTG CCA    2733
Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu Leu Leu Pro
820                 825                 830                 835

CCT GAA AAA TAC ATG AGA GTA GCA TCA CCT TCA AGA AAG GTA CAA TTC    2781
Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys Val Gln Phe
                840                 845                 850

AAC CAA AAC ACA AAT CTA AGA GTA ATC CAA AAA AAT CAA GAA GAA ACT    2829
Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln Glu Glu Thr
            855                 860                 865

ACT TCA ATT TCA AAA ATA ACT GTC AAT CCA GAC TCT GAA GAA CTT TTC    2877
Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu Glu Leu Phe
        870                 875                 880

TCA GAC AAT GAG AAT AAT TTT GTC TTC CAA GTA GCT AAT GAA AGG AAT    2925
Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn Glu Arg Asn
    885                 890                 895

AAT CTT GCT TTA GGA AAT ACT AAG GAA CTT CAT GAA ACA GAC TTG ACT    2973
Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr Asp Leu Thr
900                 905                 910                 915

TGT GTA AAC GAA CCC ATT TTC AAG AAC TCT ACC ATG GTT TTA TAT GGA    3021
Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val Leu Tyr Gly
                920                 925                 930

GAC ACA GGT GAT AAA CAA GCA ACC CAA GTG TCA ATT AAA AAA GAT TTG    3069
Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys Lys Asp Leu
            935                 940                 945

GTT TAT GTT CTT GCA GAG GAG AAC AAA AAT AGT GTA AAG CAG CAT ATA    3117
Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys Gln His Ile
        950                 955                 960

AAA ATG ACT CTA GGT CAA GAT TTA AAA TCG GAC ATC TCC TTG AAT ATA    3165
Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser Leu Asn Ile
    965                 970                 975

GAT AAA ATA CCA GAA AAA AAT AAT GAT TAC ATG GAC AAA TGG GCA GGA    3213
Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asp Lys Trp Ala Gly
980                 985                 990                 995

CTC TTA GGT CCA ATT TCA AAT CAC AGT TTT GGA GGT AGC TTC AGA ACA    3261
Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser Phe Arg Thr
                1000                1005                1010

GCT TCA AAT AAG GAA ATC AAG CTC TCT GAA CAT AAC ATT AAG AAG AGC    3309
Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile Lys Lys Ser
            1015                1020                1025

AAA ATG TTC TTC AAA GAT ATT GAA GAA CAA TAT CCT ACT AGT TTA GCT    3357
Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr Ser Leu Ala
        1030                1035                1040
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TGT GTT GAA ATT GTA AAT ACC TTG GCA TTA GAT AAT CAA AAG AAA CTG    3405
Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln Lys Lys Leu
   1045                1050                1055

AGC AAG CCT CAG TCA ATT AAT ACT GTA TCT GCA CAT TTA CAG AGT AGT    3453
Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu Gln Ser Ser
1060                1065                1070                1075

GTA GTT GTT TCT GAT TGT AAA AAT AGT CAT ATA ACC CCT CAG ATG TTA    3501
Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro Gln Met Leu
                1080                1085                1090

TTT TCC AAG CAG GAT TTT AAT TCA AAC CAT AAT TTA ACA CCT AGC CAA    3549
Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr Pro Ser Gln
           1095                1100                1105

AAG GCA GAA ATT ACA GAA CTT TCT ACT ATA TTA GAA GAA TCA GGA AGT    3597
Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu Ser Gly Ser
      1110                1115                1120

CAG TTT GAA TTT ACT CAG TTT AGA AAG CCA AGC TAC ATA TTG CAG AAG    3645
Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile Leu Gln Lys
   1125                1130                1135

AGT ACA TTT GAA GTG CCT GAA AAC CAG ATG ACT ATC TTA AAG ACC ACT    3693
Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu Lys Thr Thr
1140                1145                1150                1155

TCT GAG GAA TGC AGA GAT GCT GAT CTT CAT GTC ATA ATG AAT GCC CCA    3741
Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met Asn Ala Pro
                1160                1165                1170

TCG ATT GGT CAG GTA GAC AGC AGC AAG CAA TTT GAA GGT ACA GTT GAA    3789
Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly Thr Val Glu
           1175                1180                1185

ATT AAA CGG AAG TTT GCT GGC CTG TTG AAA AAT GAC TGT AAC AAA AGT    3837
Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys Asn Lys Ser
      1190                1195                1200

GCT TCT GGT TAT TTA ACA GAT GAA AAT GAA GTG GGG TTT AGG GGC TTT    3885
Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe Arg Gly Phe
   1205                1210                1215

TAT TCT GCT CAT GGC ACA AAA CTG AAT GTT TCT ACT GAA GCT CTG CAA    3933
Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu Ala Leu Gln
1220                1225                1230                1235

AAA GCT GTG AAA CTG TTT AGT GAT ATT GAG AAT ATT AGT GAG GAA ACT    3981
Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser Glu Glu Thr
                1240                1245                1250

TCT GCA GAG GTA CAT CCA ATA AGT TTA TCT TCA AGT AAA TGT CAT GAT    4029
Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys Cys His Asp
           1255                1260                1265

TCT GTT GTT TCA ATG TTT AAG ATA GAA AAT CAT AAT GAT AAA ACT GTA    4077
Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp Lys Thr Val
      1270                1275                1280

AGT GAA AAA AAT AAT AAA TGC CAA CTG ATA TTA CAA AAT AAT ATT GAA    4125
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      Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn Asn Ile Glu
         1285                1290                1295

 5    ATG ACT ACT GGC ACT TTT GTT GAA GAA ATT ACT GAA AAT TAC AAG AGA    4173
      Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn Tyr Lys Arg
     1300                1305                1310                1315

      AAT ACT GAA AAT GAA GAT AAC AAA TAT ACT GCT GCC AGT AGA AAT TCT    4221
10    Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser Arg Asn Ser
                    1320                1325                1330

      CAT AAC TTA GAA TTT GAT GGC AGT GAT TCA AGT AAA AAT GAT ACT GTT    4269
      His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn Asp Thr Val
15               1335                1340                1345

      TGT ATT CAT AAA GAT GAA ACG GAC TTG CTA TTT ACT GAT CAG CAC AAC    4317
      Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp Gln His Asn
            1350                1355                1360
20
      ATA TGT CTT AAA TTA TCT GGC CAG TTT ATG AAG GAG GGA AAC ACT CAG    4365
      Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly Asn Thr Gln
         1365                1370                1375

25    ATT AAA GAA GAT TTG TCA GAT TTA ACT TTT TTG GAA GTT GCG AAA GCT    4413
      Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val Ala Lys Ala
     1380                1385                1390                1395

      CAA GAA GCA TGT CAT GGT AAT ACT TCA AAT AAA GAA CAG TTA ACT GCT    4461
30    Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln Leu Thr Ala
                    1400                1405                1410

      ACT AAA ACG GAG CAA AAT ATA AAA GAT TTT GAG ACT TCT GAT ACA TTT    4509
      Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser Asp Thr Phe
35               1415                1420                1425

      TTT CAG ACT GCA AGT GGG AAA AAT ATT AGT GTC GCC AAA GAG TCA TTT    4557
      Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys Glu Ser Phe
            1430                1435                1440
40
      AAT AAA ATT GTA AAT TTC TTT GAT CAG AAA CCA GAA GAA TTG CAT AAC    4605
      Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu Leu His Asn
         1445                1450                1455

45    TTT TCC TTA AAT TCT GAA TTA CAT TCT GAC ATA AGA AAG AAC AAA ATG    4653
      Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys Asn Lys Met
     1460                1465                1470                1475

      GAC ATT CTA AGT TAT GAG GAA ACA GAC ATA GTT AAA CAC AAA ATA CTG    4701
50    Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His Lys Ile Leu
                    1480                1485                1490

      AAA GAA AGT GTC CCA GTT GGT ACT GGA AAT CAA CTA GTG ACC TTC CAG    4749
      Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val Thr Phe Gln
55               1495                1500                1505

      GGA CAA CCC GAA CGT GAT GAA AAG ATC AAA GAA CCT ACT CTG TTG GGT    4797
      Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr Leu Leu Gly
            1510                1515                1520
60
      TTT CAT ACA GCT AGC GGG AAA AAA GTT AAA ATT GCA AAG GAA TCT TTG    4845
      Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys Glu Ser Leu
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      1525                1530                1535

   GAC AAA GTG AAA AAC CTT TTT GAT GAA AAA GAG CAA GGT ACT AGT GAA    4893
5  Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly Thr Ser Glu
  1540                1545                1550                1555

   ATC ACC AGT TTT AGC CAT CAA TGG GCA AAG ACC CTA AAG TAC AGA GAG    4941
   Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys Tyr Arg Glu
10                1560                1565                1570

   GCC TGT AAA GAC CTT GAA TTA GCA TGT GAG ACC ATT GAG ATC ACA GCT    4989
   Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu Ile Thr Ala
            1575                1580                1585
15
   GCC CCA AAG TGT AAA GAA ATG CAG AAT TCT CTC AAT AAT GAT AAA AAC    5037
   Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn Asp Lys Asn
         1590                1595                1600

20 CTT GTT TCT ATT GAG ACT GTG GTG CCA CCT AAG CTC TTA AGT GAT AAT    5085
   Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu Ser Asp Asn
      1605                1610                1615

   TTA TGT AGA CAA ACT GAA AAT CTC AAA ACA TCA AAA AGT ATC TTT TTG    5133
25 Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser Ile Phe Leu
  1620                1625                1630                1635

   AAA GTT AAA GTA CAT GAA AAT GTA GAA AAA GAA ACA GCA AAA AGT CCT    5181
   Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala Lys Ser Pro
30                1640                1645                1650

   GCA ACT TGT TAC ACA AAT CAG TCC CCT TAT TCA GTC ATT GAA AAT TCA    5229
   Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile Glu Asn Ser
            1655                1660                1665
35
   GCC TTA GCT TTT TAC ACA AGT TGT AGT AGA AAA ACT TCT GTG AGT CAG    5277
   Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser Val Ser Gln
         1670                1675                1680

40 ACT TCA TTA CTT GAA GCA AAA AAA TGG CTT AGA GAA GGA ATA TTT GAT    5325
   Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly Ile Phe Asp
      1685                1690                1695

   GGT CAA CCA GAA AGA ATA AAT ACT GCA GAT TAT GTA GGA AAT TAT TTG    5373
45 Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly Asn Tyr Leu
  1700                1705                1710                1715

   TAT GAA AAT AAT TCA AAC AGT ACT ATA GCT GAA AAT GAC AAA AAT CAT    5421
   Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp Lys Asn His
50                1720                1725                1730

   CTC TCC GAA AAA CAA GAT ACT TAT TTA AGT AAC AGT AGC ATG TCT AAC    5469
   Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser Met Ser Asn
            1735                1740                1745
55
   AGC TAT TCC TAC CAT TCT GAT GAG GTA TAT AAT GAT TCA GGA TAT CTC    5517
   Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser Gly Tyr Leu
         1750                1755                1760

60 TCA AAA AAT AAA CTT GAT TCT GGT ATT GAG CCA GTA TTG AAG AAT GTT    5565
   Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu Lys Asn Val
      1765                1770                1775
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GAA GAT CAA AAA AAC ACT AGT TTT TCC AAA GTA ATA TCC AAT GTA AAA 5613
Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser Asn Val Lys
1780 1785 1790 1795

GAT GCA AAT GCA TAC CCA CAA ACT GTA AAT GAA GAT ATT TGC GTT GAG 5661
Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile Cys Val Glu
1800 1805 1810

GAA CTT GTG ACT AGC TCT TCA CCC TGC AAA AAT AAA AAT GCA GCC ATT 5709
Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn Ala Ala Ile
1815 1820 1825

AAA TTG TCC ATA TCT AAT AGT AAT AAT TTT GAG GTA GGG CCA CCT GCA 5757
Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly Pro Pro Ala
1830 1835 1840

TTT AGG ATA GCC AGT GGT AAA ATC GTT TGT GTT TCA CAT GAA ACA ATT 5805
Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His Glu Thr Ile
1845 1850 1855

AAA AAA GTG AAA GAC ATA TTT ACA GAC AGT TTC AGT AAA GTA ATT AAG 5853
Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys Val Ile Lys
1860 1865 1870 1875

GAA AAC AAC GAG AAT AAA TCA AAA ATT TGC CAA ACG AAA ATT ATG GCA 5901
Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys Ile Met Ala
1880 1885 1890

GGT TGT TAC GAG GCA TTG GAT GAT TCA GAG GAT ATT CTT CAT AAC TCT 5949
Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu His Asn Ser
1895 1900 1905

CTA GAT AAT GAT GAA TGT AGC ACG CAT TCA CAT AAG GTT TTT GCT GAC 5997
Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val Phe Ala Asp
1910 1915 1920

ATT CAG AGT GAA GAA ATT TTA CAA CAT AAC CAA AAT ATG TCT GGA TTG 6045
Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met Ser Gly Leu
1925 1930 1935

GAG AAA GTT TCT AAA ATA TCA CCT TGT GAT GTT AGT TTG GAA ACT TCA 6093
Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu Glu Thr Ser
1940 1945 1950 1955

GAT ATA TGT AAA TGT AGT ATA GGG AAG CTT CAT AAG TCA GTC TCA TCT 6141
Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser Val Ser Ser
1960 1965 1970

GCA AAT ACT TGT GGG ATT TTT AGC ACA GCA AGT GGA AAA TCT GTC CAG 6189
Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys Ser Val Gln
1975 1980 1985

GTA TCA GAT GCT TCA TTA CAA AAC GCA AGA CAA GTG TTT TCT GAA ATA 6237
Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe Ser Glu Ile
1990 1995 2000

GAA GAT AGT ACC AAG CAA GTC TTT TCC AAA GTA TTG TTT AAA AGT AAC 6285
Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe Lys Ser Asn
2005 2010 2015

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GAA CAT TCA GAC CAG CTC ACA AGA GAA GAA AAT ACT GCT ATA CGT ACT    6333
Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala Ile Arg Thr
2020                2025                2030                2035

CCA GAA CAT TTA ATA TCC CAA AAA GGC TTT TCA TAT AAT GTG GTA AAT    6381
Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn Val Val Asn
                2040                2045                2050

TCA TCT GCT TTC TCT GGA TTT AGT ACA GCA AGT GGA AAG CAA GTT TCC    6429
Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys Gln Val Ser
            2055                2060                2065

ATT TTA GAA AGT TCC TTA CAC AAA GTT AAG GGA GTG TTA GAG GAA TTT    6477
Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu Glu Glu Phe
        2070                2075                2080

GAT TTA ATC AGA ACT GAG CAT AGT CTT CAC TAT TCA CCT ACG TCT AGA    6525
Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro Thr Ser Arg
    2085                2090                2095

CAA AAT GTA TCA AAA ATA CTT CCT CGT GTT GAT AAG AGA AAC CCA GAG    6573
Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg Asn Pro Glu
2100                2105                2110                2115

CAC TGT GTA AAC TCA GAA ATG GAA AAA ACC TGC AGT AAA GAA TTT AAA    6621
His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys Glu Phe Lys
                2120                2125                2130

TTA TCA AAT AAC TTA AAT GTT GAA GGT GGT TCT TCA GAA AAT AAT CAC    6669
Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu Asn Asn His
            2135                2140                2145

TCT ATT AAA GTT TCT CCA TAT CTC TCT CAA TTT CAA CAA GAC AAA CAA    6717
Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln Asp Lys Gln
        2150                2155                2160

CAG TTG GTA TTA GGA ACC AAA GTC TCA CTT GTT GAG AAC ATT CAT GTT    6765
Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn Ile His Val
    2165                2170                2175

TTG GGA AAA GAA CAG GCT TCA CCT AAA AAC GTA AAA ATG GAA ATT GGT    6813
Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met Glu Ile Gly
2180                2185                2190                2195

AAA ACT GAA ACT TTT TCT GAT GTT CCT GTG AAA ACA AAT ATA GAA GTT    6861
Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn Ile Glu Val
                2200                2205                2210

TGT TCT ACT TAC TCC AAA GAT TCA GAA AAC TAC TTT GAA ACA GAA GCA    6909
Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu Thr Glu Ala
            2215                2220                2225

GTA GAA ATT GCT AAA GCT TTT ATG GAA GAT GAT GAA CTG ACA GAT TCT    6957
Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu Thr Asp Ser
        2230                2235                2240

AAA CTG CCA AGT CAT GCC ACA CAT TCT CTT TTT ACA TGT CCC GAA AAT    7005
Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys Pro Glu Asn
    2245                2250                2255

GAG GAA ATG GTT TTG TCA AAT TCA AGA ATT GGA AAA AGA AGA GGA GAG    7053
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Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg Arg Gly Glu
2260                2265                2270                2275

CCC CTT ATC TTA GTG GGA GAA CCC TCA ATC AAA AGA AAC TTA TTA AAT    7101
Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn Leu Leu Asn
                2280                2285                2290

GAA TTT GAC AGG ATA ATA GAA AAT CAA GAA AAA TCC TTA AAG GCT TCA    7149
Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu Lys Ala Ser
            2295                2300                2305

AAA AGC ACT CCA GAT GGC ACA ATA AAA GAT CGA AGA TTG TTT ATG CAT    7197
Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu Phe Met His
        2310                2315                2320

CAT GTT TCT TTA GAG CCG ATT ACC TGT GTA CCC TTT CGC ACA ACT AAG    7245
His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg Thr Thr Lys
    2325                2330                2335

GAA CGT CAA GAG ATA CAG AAT CCA AAT TTT ACC GCA CCT GGT CAA GAA    7293
Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro Gly Gln Glu
2340                2345                2350                2355

TTT CTG TCT AAA TCT CAT TTG TAT GAA CAT CTG ACT TTG GAA AAA TCT    7341
Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu Glu Lys Ser
                2360                2365                2370

TCA AGC AAT TTA GCA GTT TCA GGA CAT CCA TTT TAT CAA GTT TCT GCT    7389
Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln Val Ser Ala
            2375                2380                2385

ACA AGA AAT GAA AAA ATG AGA CAC TTG ATT ACT ACA GGC AGA CCA ACC    7437
Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly Arg Pro Thr
        2390                2395                2400

AAA GTC TTT GTT CCA CCT TTT AAA ACT AAA TCG CAT TTT CAC AGA GTT    7485
Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe His Arg Val
    2405                2410                2415

GAA CAG TGT GTT AGG AAT ATT AAC TTG GAG GAA AAC AGA CAA AAG CAA    7533
Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg Gln Lys Gln
2420                2425                2430                2435

AAC ATT GAT GGA CAT GGC TCT GAT GAT AGT AAA AAT AAG ATT AAT GAC    7581
Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys Ile Asn Asp
                2440                2445                2450

AAT GAG ATT CAT CAG TTT AAC AAA AAC AAC TCC AAT CAA GCA GCA GCT    7629
Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln Ala Ala Ala
            2455                2460                2465

GTA ACT TTC ACA AAG TGT GAA GAA GAA CCT TTA GAT TTA ATT ACA AGT    7677
Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu Ile Thr Ser
        2470                2475                2480

CTT CAG AAT GCC AGA GAT ATA CAG GAT ATG CGA ATT AAG AAG AAA CAA    7725
Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys Lys Lys Gln
    2485                2490                2495

AGG CAA CGC GTC TTT CCA CAG CCA GGC AGT CTG TAT CTT GCA AAA ACA    7773
Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu Ala Lys Thr
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2500                2505                2510                2515

     TCC ACT CTG CCT CGA ATC TCT CTG AAA GCA GCA GTA GGA GGC CAA GTT    7821
5    Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly Gly Gln Val
                  2520                2525                2530

     CCC TCT GCG TGT TCT CAT AAA CAG CTG TAT ACG TAT GGC GTT TCT AAA    7869
     Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly Val Ser Lys
10             2535                2540                2545

     CAT TGC ATA AAA ATT AAC AGC AAA AAT GCA GAG TCT TTT CAG TTT CAC    7917
     His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe Gln Phe His
           2550                2555                2560
15
     ACT GAA GAT TAT TTT GGT AAG GAA AGT TTA TGG ACT GGA AAA GGA ATA    7965
     Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly Lys Gly Ile
        2565                2570                2575

20   CAG TTG GCT GAT GGT GGA TGG CTC ATA CCC TCC AAT GAT GGA AAG GCT    8013
     Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp Gly Lys Ala
     2580                2585                2590                2595

     GGA AAA GAA GAA TTT TAT AGG GCT CTG TGT GAC ACT CCA GGT GTG GAT    8061
25   Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro Gly Val Asp
                  2600                2605                2610

     CCA AAG CTT ATT TCT AGA ATT TGG GTT TAT AAT CAC TAT AGA TGG ATC    8109
     Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr Arg Trp Ile
30             2615                2620                2625

     ATA TGG AAA CTG GCA GCT ATG GAA TGT GCC TTT CCT AAG GAA TTT GCT    8157
     Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys Glu Phe Ala
           2630                2635                2640
35
     AAT AGA TGC CTA AGC CCA GAA AGG GTG CTT CTT CAA CTA AAA TAC AGA    8205
     Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu Lys Tyr Arg
        2645                2650                2655

40   TAT GAT ACG GAA ATT GAT AGA AGC AGA AGA TCG GCT ATA AAA AAG ATA    8253
     Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile Lys Lys Ile
     2660                2665                2670                2675

     ATG GAA AGG GAT GAC ACA GCT GCA AAA ACA CTT GTT CTC TGT GTT TCT    8301
45   Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu Cys Val Ser
                  2680                2685                2690

     GAC ATA ATT TCA TTG AGC GCA AAT ATA TCT GAA ACT TCT AGC AAT AAA    8349
     Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser Ser Asn Lys
50             2695                2700                2705

     ACT AGT AGT GCA GAT ACC CAA AAA GTG GCC ATT ATT GAA CTT ACA GAT    8397
     Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu Leu Thr Asp
           2710                2715                2720
55
     GGG TGG TAT GCT GTT AAG GCC CAG TTA GAT CCT CCC CTC TTA GCT GTC    8445
     Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu Leu Ala Val
        2725                2730                2735

60   TTA AAG AAT GGC AGA CTG ACA GTT GGT CAG AAG ATT ATT CTT CAT GGA    8493
     Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile Leu His Gly
     2740                2745                2750                2755
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GCA GAA CTG GTG GGC TCT CCT GAT GCC TGT ACA CCT CTT GAA GCC CCA    8541
Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu Glu Ala Pro
                2760                2765                2770

GAA TCT CTT ATG TTA AAG ATT TCT GCT AAC AGT ACT CGG CCT GCT CGC    8589
Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg Pro Ala Arg
            2775                2780                2785

TGG TAT ACC AAA CTT GGA TTC TTT CCT GAC CCT AGA CCT TTT CCT CTG    8637
Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro Phe Pro Leu
        2790                2795                2800

CCC TTA TCA TCG CTT TTC AGT GAT GGA GGA AAT GTT GGT TGT GTT GAT    8685
Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly Cys Val Asp
    2805                2810                2815

GTA ATT ATT CAA AGA GCA TAC CCT ATA CAG TGG ATG GAG AAG ACA TCA    8733
Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu Lys Thr Ser
2820                2825                2830                2835

TCT GGA TTA TAC ATA TTT CGC AAT GAA AGA GAG GAA GAA AAG GAA GCA    8781
Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu Lys Glu Ala
                2840                2845                2850

GCA AAA TAT GTG GAG GCC CAA CAA AAG AGA CTA GAA GCC TTA TTC ACT    8829
Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala Leu Phe Thr
            2855                2860                2865

AAA ATT CAG GAG GAA TTT GAA GAA CAT GAA GAA AAC ACA ACA AAA CCA    8877
Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr Thr Lys Pro
        2870                2875                2880

TAT TTA CCA TCA CGT GCA CTA ACA AGA CAG CAA GTT CGT GCT TTG CAA    8925
Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg Ala Leu Gln
    2885                2890                2895

GAT GGT GCA GAG CTT TAT GAA GCA GTG AAG AAT GCA GCA GAC CCA GCT    8973
Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala Asp Pro Ala
2900                2905                2910                2915

TAC CTT GAG GGT TAT TTC AGT GAA GAG CAG TTA AGA GCC TTG AAT AAT    9021
Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala Leu Asn Asn
                2920                2925                2930

CAC AGG CAA ATG TTG AAT GAT AAG AAA CAA GCT CAG ATC CAG TTG GAA    9069
His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile Gln Leu Glu
            2935                2940                2945

ATT AGG AAG GCC ATG GAA TCT GCT GAA CAA AAG GAA CAA GGT TTA TCA    9117
Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln Gly Leu Ser
        2950                2955                2960

AGG GAT GTC ACA ACC GTG TGG AAG TTG CGT ATT GTA AGC TAT TCA AAA    9165
Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser Tyr Ser Lys
    2965                2970                2975

AAA GAA AAA GAT TCA GTT ATA CTG AGT ATT TGG CGT CCA TCA TCA GAT    9213
Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro Ser Ser Asp
2980                2985                2990                2995
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TTA TAT TCT CTG TTA ACA GAA GGA AAG AGA TAC AGA ATT TAT CAT CTT    9261
Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile Tyr His Leu
                3000                3005                3010

GCA ACT TCA AAA TCT AAA AGT AAA TCT GAA AGA GCT AAC ATA CAG TTA    9309
Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn Ile Gln Leu
            3015                3020                3025

GCA GCG ACA AAA AAA ACT CAG TAT CAA CAA CTA CCG GTT TCA GAT GAA    9357
Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val Ser Asp Glu
        3030                3035                3040

ATT TTA TTT CAG ATT TAC CAG CCA CGG GAG CCC CTT CAC TTC AGC AAA    9405
Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His Phe Ser Lys
    3045                3050                3055

TTT TTA GAT CCA GAC TTT CAG CCA TCT TGT TCT GAG GTG GAC CTA ATA    9453
Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val Asp Leu Ile
3060                3065                3070                3075

GGA TTT GTC GTT TCT GTT GTG AAA AAA ACA GGA CTT GCC CCT TTC GTC    9501
Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala Pro Phe Val
                3080                3085                3090

TAT TTG TCA GAC GAA TGT TAC AAT TTA CTG GCA ATA AAG TTT TGG ATA    9549
Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys Phe Trp Ile
            3095                3100                3105

GAC CTT AAT GAG GAC ATT ATT AAG CCT CAT ATG TTA ATT GCT GCA AGC    9597
Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile Ala Ala Ser
        3110                3115                3120

AAC CTC CAG TGG CGA CCA GAA TCC AAA TCA GGC CTT CTT ACT TTA TTT    9645
Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu Thr Leu Phe
    3125                3130                3135

GCT GGA GAT TTT TCT GTG TTT TCT GCT AGT CCA AAA GAG GGC CAC TTT    9693
Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu Gly His Phe
3140                3145                3150                3155

CAA GAG ACA TTC AAC AAA ATG AAA AAT ACT GTT GAG AAT ATT GAC ATA    9741
Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn Ile Asp Ile
                3160                3165                3170

CTT TGC AAT GAA GCA GAA AAC AAG CTT ATG CAT ATA CTG CAT GCA AAT    9789
Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu His Ala Asn
            3175                3180                3185

GAT CCC AAG TGG TCC ACC CCA ACT AAA GAC TGT ACT TCA GGG CCG TAC    9837
Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser Gly Pro Tyr
        3190                3195                3200

ACT GCT CAA ATC ATT CCT GGT ACA GGA AAC AAG CTT CTG ATG TCT TCT    9885
Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu Met Ser Ser
    3205                3210                3215

CCT AAT TGT GAG ATA TAT TAT CAA AGT CCT TTA TCA CTT TGT ATG GCC    9933
Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu Cys Met Ala
3220                3225                3230                3235

AAA AGG AAG TCT GTT TCC ACA CCT GTC TCA GCC CAG ATG ACT TCA AAG    9981
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Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met Thr Ser Lys
                3240                3245                3250

TCT TGT AAA GGG GAG AAA GAG ATT GAT GAC CAA AAG AAC TGC AAA AAG   10029
Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn Cys Lys Lys
           3255                3260                3265

AGA AGA GCC TTG GAT TTC TTG AGT AGA CTG CCT TTA CCT CCA CCT GTT   10077
Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro Pro Pro Val
       3270                3275                3280

AGT CCC ATT TGT ACA TTT GTT TCT CCG GCT GCA CAG AAG GCA TTT CAG   10125
Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys Ala Phe Gln
   3285                3290                3295

CCA CCA AGG AGT TGT GGC ACC AAA TAC GAA ACA CCC ATA AAG AAA AAA   10173
Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile Lys Lys Lys
3300                3305                3310                3315

GAA CTG AAT TCT CCT CAG ATG ACT CCA TTT AAA AAA TTC AAT GAA ATT   10221
Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe Asn Glu Ile
                3320                3325                3330

TCT CTT TTG GAA AGT AAT TCA ATA GCT GAC GAA GAA CTT GCA TTG ATA   10269
Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile
           3335                3340                3345

AAT ACC CAA GCT CTT TTG TCT GGT TCA ACA GGA GAA AAA CAA TTT ATA   10317
Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys Gln Phe Ile
       3350                3355                3360

TCT GTC AGT GAA TCC ACT AGG ACT GCT CCC ACC AGT TCA GAA GAT TAT   10365
Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp Tyr
   3365                3370                3375

CTC AGA CTG AAA CGA CGT TGT ACT ACA TCT CTG ATC AAA GAA CAG GAG   10413
Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu Gln Glu
3380                3385                3390                3395

AGT TCC CAG GCC AGT ACG GAA GAA TGT GAG AAA AAT AAG CAG GAC ACA   10461
Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys Gln Asp Thr
                3400                3405                3410

ATT ACA ACT AAA AAA TAT ATC TAA                                  10485
Ile Thr Thr Lys Lys Tyr Ile
           3415
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(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3418 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

Met Pro Ile Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys
1 5 10 15
Thr Arg Cys Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe
20 25 30
Glu Glu Leu Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu
35 40 45
Glu Ser Glu His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr
50 55 60
Pro Gln Arg Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile
65 70 75 80
Phe Lys Glu Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys
85 90 95
Glu Leu Asp Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser
100 105 110
Arg His Lys Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp
115 120 125
Asp Val Ser Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val
130 135 140
Val Leu Gln Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val
145 150 155 160
Cys Gly Ser Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr
165 170 175
Pro Lys His Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met
180 185 190
Ser Trp Ser Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val
195 200 205
Leu Ile Val Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp
210 215 220
Thr Thr Ala Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu
225 230 235 240
Lys Lys Asn Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr
245 250 255
Asn Gln Arg Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn
260 265 270
Ser Phe Lys Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro
275 280 285
His Val Leu Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu
290 295 300
Glu Asp Ser Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu
305 310 315 320
Gln Lys Val Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala
325 330 335
Asn Ala Asp Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr
340 345 350
Ser Phe Val Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser
355 360 365
Asn Val Ala Asn Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser
370 375 380
Lys Glu Val Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu
385 390 395 400
Ser Gly Leu Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile
405 410 415
Ser Ser Cys Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu
420 425 430
Asn Lys Arg Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg
435 440 445
Ile Ser Ser Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val
450 455 460
Val Asn Lys Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys
465 470 475 480
Ile Leu Ala Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser

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                    485                 490                 495
Ser Phe Gln Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro
                500                 505                 510
Lys Glu Thr Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn
            515                 520                 525
Phe Lys Lys Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr
        530                 535                 540
Val Cys Ser Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn
545                 550                 555                 560
Gly Ser Trp Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn
                565                 570                 575
Ala Gly Leu Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr
            580                 585                 590
Ala Ile His Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp
        595                 600                 605
Gln Lys Ser Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala
    610                 615                 620
Phe Glu Ala Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His
625                 630                 635                 640
Ser Ser Val Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr
                645                 650                 655
Leu Ser Leu Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg
            660                 665                 670
Asn Glu Thr Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr
        675                 680                 685
Lys Glu Ala Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro
    690                 695                 700
Glu Ala Asp Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp
705                 710                 715                 720
Pro Lys Ser Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala
                725                 730                 735
Ala Cys His Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp
            740                 745                 750
Phe Gln Ser Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr
        755                 760                 765
Leu Ile Leu Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met
    770                 775                 780
Ile Ser Arg Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly
785                 790                 795                 800
Asn Asn Tyr Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu
                805                 810                 815
Lys Asn Gln Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu
            820                 825                 830
Leu Leu Pro Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys
        835                 840                 845
Val Gln Phe Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln
    850                 855                 860
Glu Glu Thr Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu
865                 870                 875                 880
Glu Leu Phe Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn
                885                 890                 895
Glu Arg Asn Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr
            900                 905                 910
Asp Leu Thr Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val
        915                 920                 925
Leu Tyr Gly Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys
    930                 935                 940
Lys Asp Leu Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys
945                 950                 955                 960
Gln His Ile Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser
                965                 970                 975
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Leu Asn Ile Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asp Lys
980 985 990
Trp Ala Gly Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser
995 1000 1005
Phe Arg Thr Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile
1010 1015 1020
Lys Lys Ser Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr
1025 1030 1035 104
Ser Leu Ala Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln
1045 1050 1055
Lys Lys Leu Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu
1060 1065 1070
Gln Ser Ser Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro
1075 1080 1085
Gln Met Leu Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr
1090 1095 1100
Pro Ser Gln Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu
1105 1110 1115 112
Ser Gly Ser Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile
1125 1130 1135
Leu Gln Lys Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu
1140 1145 1150
Lys Thr Thr Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met
1155 1160 1165
Asn Ala Pro Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly
1170 1175 1180
Thr Val Glu Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys
1185 1190 1195 120
Asn Lys Ser Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe
1205 1210 1215
Arg Gly Phe Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu
1220 1225 1230
Ala Leu Gln Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser
1235 1240 1245
Glu Glu Thr Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys
1250 1255 1260
Cys His Asp Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp
1265 1270 1275 128
Lys Thr Val Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn
1285 1290 1295
Asn Ile Glu Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn
1300 1305 1310
Tyr Lys Arg Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser
1315 1320 1325
Arg Asn Ser His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn
1330 1335 1340
Asp Thr Val Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp
1345 1350 1355 136
Gln His Asn Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly
1365 1370 1375
Asn Thr Gln Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val
1380 1385 1390
Ala Lys Ala Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln
1395 1400 1405
Leu Thr Ala Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser
1410 1415 1420
Asp Thr Phe Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys
1425 1430 1435 144
Glu Ser Phe Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu
1445 1450 1455
Leu His Asn Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys

1460 1465 1470
Asn Lys Met Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His
1475 1480 1485
Lys Ile Leu Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val
1490 1495 1500
Thr Phe Gln Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr
1505 1510 1515 152
Leu Leu Gly Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys
1525 1530 1535
Glu Ser Leu Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly
1540 1545 1550
Thr Ser Glu Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys
1555 1560 1565
Tyr Arg Glu Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu
1570 1575 1580
Ile Thr Ala Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn
1585 1590 1595 160
Asp Lys Asn Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu
1605 1610 1615
Ser Asp Asn Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser
1620 1625 1630
Ile Phe Leu Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala
1635 1640 1645
Lys Ser Pro Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile
1650 1655 1660
Glu Asn Ser Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser
1665 1670 1675 168
Val Ser Gln Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly
1685 1690 1695
Ile Phe Asp Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly
1700 1705 1710
Asn Tyr Leu Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp
1715 1720 1725
Lys Asn His Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser
1730 1735 1740
Met Ser Asn Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser
1745 1750 1755 176
Gly Tyr Leu Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu
1765 1770 1775
Lys Asn Val Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser
1780 1785 1790
Asn Val Lys Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile
1795 1800 1805
Cys Val Glu Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn
1810 1815 1820
Ala Ala Ile Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly
1825 1830 1835 184
Pro Pro Ala Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His
1845 1850 1855
Glu Thr Ile Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys
1860 1865 1870
Val Ile Lys Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys
1875 1880 1885
Ile Met Ala Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu
1890 1895 1900
His Asn Ser Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val
1905 1910 1915 192
Phe Ala Asp Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met
1925 1930 1935
Ser Gly Leu Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu
1940 1945 1950

Glu Thr Ser Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser
1955 1960 1965
Val Ser Ser Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys
1970 1975 1980
Ser Val Gln Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe
1985 1990 1995 200
Ser Glu Ile Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe
2005 2010 2015
Lys Ser Asn Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala
2020 2025 2030
Ile Arg Thr Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn
2035 2040 2045
Val Val Asn Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys
2050 2055 2060
Gln Val Ser Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu
2065 2070 2075 208
Glu Glu Phe Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro
2085 2090 2095
Thr Ser Arg Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg
2100 2105 2110
Asn Pro Glu His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys
2115 2120 2125
Glu Phe Lys Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu
2130 2135 2140
Asn Asn His Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln
2145 2150 2155 216
Asp Lys Gln Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn
2165 2170 2175
Ile His Val Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met
2180 2185 2190
Glu Ile Gly Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn
2195 2200 2205
Ile Glu Val Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu
2210 2215 2220
Thr Glu Ala Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu
2225 2230 2235 224
Thr Asp Ser Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys
2245 2250 2255
Pro Glu Asn Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg
2260 2265 2270
Arg Gly Glu Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn
2275 2280 2285
Leu Leu Asn Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu
2290 2295 2300
Lys Ala Ser Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu
2305 2310 2315 232
Phe Met His His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg
2325 2330 2335
Thr Thr Lys Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro
2340 2345 2350
Gly Gln Glu Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu
2355 2360 2365
Glu Lys Ser Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln
2370 2375 2380
Val Ser Ala Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly
2385 2390 2395 240
Arg Pro Thr Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe
2405 2410 2415
His Arg Val Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg
2420 2425 2430
Gln Lys Gln Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys

2435 2440 2445

Ile Asn Asp Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln
2450 2455 2460

Ala Ala Ala Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu
2465 2470 2475 248

Ile Thr Ser Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys
2485 2490 2495

Lys Lys Gln Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu
2500 2505 2510

Ala Lys Thr Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly
2515 2520 2525

Gly Gln Val Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly
2530 2535 2540

Val Ser Lys His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe
2545 2550 2555 256

Gln Phe His Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly
2565 2570 2575

Lys Gly Ile Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp
2580 2585 2590

Gly Lys Ala Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro
2595 2600 2605

Gly Val Asp Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr
2610 2615 2620

Arg Trp Ile Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys
2625 2630 2635 264

Glu Phe Ala Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu
2645 2650 2655

Lys Tyr Arg Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile
2660 2665 2670

Lys Lys Ile Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu
2675 2680 2685

Cys Val Ser Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser
2690 2695 2700

Ser Asn Lys Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu
2705 2710 2715 272

Leu Thr Asp Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu
2725 2730 2735

Leu Ala Val Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile
2740 2745 2750

Leu His Gly Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu
2755 2760 2765

Glu Ala Pro Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg
2770 2775 2780

Pro Ala Arg Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro
2785 2790 2795 280

Phe Pro Leu Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly
2805 2810 2815

Cys Val Asp Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu
2820 2825 2830

Lys Thr Ser Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu
2835 2840 2845

Lys Glu Ala Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala
2850 2855 2860

Leu Phe Thr Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr
2865 2870 2875 288

Thr Lys Pro Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg
2885 2890 2895

Ala Leu Gln Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala
2900 2905 2910

Asp Pro Ala Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala
2915 2920 2925

Leu Asn Asn His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile
2930 2935 2940
Gln Leu Glu Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln
2945 2950 2955 296
Gly Leu Ser Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser
2965 2970 2975
Tyr Ser Lys Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro
2980 2985 2990
Ser Ser Asp Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile
2995 3000 3005
Tyr His Leu Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn
3010 3015 3020
Ile Gln Leu Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val
3025 3030 3035 304
Ser Asp Glu Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His
3045 3050 3055
Phe Ser Lys Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val
3060 3065 3070
Asp Leu Ile Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala
3075 3080 3085
Pro Phe Val Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys
3090 3095 3100
Phe Trp Ile Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile
3105 3110 3115 312
Ala Ala Ser Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu
3125 3130 3135
Thr Leu Phe Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu
3140 3145 3150
Gly His Phe Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn
3155 3160 3165
Ile Asp Ile Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu
3170 3175 3180
His Ala Asn Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser
3185 3190 3195 320
Gly Pro Tyr Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu
3205 3210 3215
Met Ser Ser Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu
3220 3225 3230
Cys Met Ala Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met
3235 3240 3245
Thr Ser Lys Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn
3250 3255 3260
Cys Lys Lys Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro
3265 3270 3275 328
Pro Pro Val Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys
3285 3290 3295
Ala Phe Gln Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile
3300 3305 3310
Lys Lys Lys Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe
3315 3320 3325
Asn Glu Ile Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu
3330 3335 3340
Ala Leu Ile Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys
3345 3350 3355 336
Gln Phe Ile Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser
3365 3370 3375
Glu Asp Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys
3380 3385 3390
Glu Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys
3395 3400 3405
Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile

3410 3415

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10485 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 229...10482
(D) OTHER INFORMATION: BRCA2 (OMI4)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

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GGTGGCGCGA GCTTCTGAAA CTAGGCGGCA GAGGCGGAGC CGCTGTGGCA CTGCTGCGCC     60
TCTGCTGCGC CTCGGGTGTC TTTTGCGGCG GTGGGTCGCC GCCGGGAGAA GCGTGAGGGG    120
ACAGATTTGT GACCGGCGCG GTTTTTGTCA GCTTACTCCG GCCAAAAAAG AACTGCACCT    180
CTGGAGCGGA CTTATTTACC AAGCATTGGA GGAATATCGT AGGTAAAA ATG CCT ATT     237
                                                      Met Pro Ile
                                                       1

GGA TCC AAA GAG AGG CCA ACA TTT TTT GAA ATT TTT AAG ACA CGC TGC      285
Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys Thr Arg Cys
 5                  10                  15

AAC AAA GCA GAT TTA GGA CCA ATA AGT CTT AAT TGG TTT GAA GAA CTT      333
Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe Glu Glu Leu
20                  25                  30                  35

TCT TCA GAA GCT CCA CCC TAT AAT TCT GAA CCT GCA GAA GAA TCT GAA      381
Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu Glu Ser Glu
                40                  45                  50

CAT AAA AAC AAC AAT TAC GAA CCA AAC CTA TTT AAA ACT CCA CAA AGG      429
His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr Pro Gln Arg
            55                  60                  65

AAA CCA TCT TAT AAT CAG CTG GCT TCA ACT CCA ATA ATA TTC AAA GAG      477
Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile Phe Lys Glu
        70                  75                  80

CAA GGG CTG ACT CTG CCG CTG TAC CAA TCT CCT GTA AAA GAA TTA GAT      525
Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys Glu Leu Asp
    85                  90                  95

AAA TTC AAA TTA GAC TTA GGA AGG AAT GTT CCC AAT AGT AGA CAT AAA      573
Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser Arg His Lys
100                 105                 110                 115

AGT CTT CGC ACA GTG AAA ACT AAA ATG GAT CAA GCA GAT GAT GTT TCC      621
Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp Asp Val Ser
                120                 125                 130

TGT CCA CTT CTA AAT TCT TGT CTT AGT GAA AGT CCT GTT GTT CTA CAA      669
Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val Val Leu Gln
            135                 140                 145
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TGT ACA CAT GTA ACA CCA CAA AGA GAT AAG TCA GTG GTA TGT GGG AGT      717
Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val Cys Gly Ser
        150                 155                 160

TTG TTT CAT ACA CCA AAG TTT GTG AAG GGT CGT CAG ACA CCA AAA CAT      765
Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr Pro Lys His
    165                 170                 175

ATT TCT GAA AGT CTA GGA GCT GAG GTG GAT CCT GAT ATG TCT TGG TCA      813
Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met Ser Trp Ser
180                 185                 190                 195

AGT TCT TTA GCT ACA CCA CCC ACC CTT AGT TCT ACT GTG CTC ATA GTC      861
Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val Leu Ile Val
                200                 205                 210

AGA AAT GAA GAA GCA TCT GAA ACT GTA TTT CCT CAT GAT ACT ACT GCT      909
Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp Thr Thr Ala
            215                 220                 225

AAT GTG AAA AGC TAT TTT TCC AAT CAT GAT GAA AGT CTG AAG AAA AAT      957
Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu Lys Lys Asn
        230                 235                 240

GAT AGA TTT ATC GCT TCT GTG ACA GAC AGT GAA AAC ACA AAT CAA AGA     1005
Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr Asn Gln Arg
    245                 250                 255

GAA GCT GCA AGT CAT GGA TTT GGA AAA ACA TCA GGG AAT TCA TTT AAA     1053
Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn Ser Phe Lys
260                 265                 270                 275

GTA AAT AGC TGC AAA GAC CAC ATT GGA AAG TCA ATG CCA AAT GTC CTA     1101
Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro Asn Val Leu
                280                 285                 290

GAA GAT GAA GTA TAT GAA ACA GTT GTA GAT ACC TCT GAA GAA GAT AGT     1149
Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu Glu Asp Ser
            295                 300                 305

TTT TCA TTA TGT TTT TCT AAA TGT AGA ACA AAA AAT CTA CAA AAA GTA     1197
Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu Gln Lys Val
        310                 315                 320

AGA ACT AGC AAG ACT AGG AAA AAA ATT TTC CAT GAA GCA AAC GCT GAT     1245
Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala Asn Ala Asp
    325                 330                 335

GAA TGT GAA AAA TCT AAA AAC CAA GTG AAA GAA AAA TAC TCA TTT GTA     1293
Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr Ser Phe Val
340                 345                 350                 355

TCT GAA GTG GAA CCA AAT GAT ACT GAT CCA TTA GAT TCA AAT GTA GCA     1341
Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser Asn Val Ala
                360                 365                 370

CAT CAG AAG CCC TTT GAG AGT GGA AGT GAC AAA ATC TCC AAG GAA GTT     1389
His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser Lys Glu Val
            375                 380                 385
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GTA CCG TCT TTG GCC TGT GAA TGG TCT CAA CTA ACC CTT TCA GGT CTA    1437
Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu Ser Gly Leu
        390                 395                 400

AAT GGA GCC CAG ATG GAG AAA ATA CCC CTA TTG CAT ATT TCT TCA TGT    1485
Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile Ser Ser Cys
    405                 410                 415

GAC CAA AAT ATT TCA GAA AAA GAC CTA TTA GAC ACA GAG AAC AAA AGA    1533
Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu Asn Lys Arg
420                 425                 430                 435

AAG AAA GAT TTT CTT ACT TCA GAG AAT TCT TTG CCA CGT ATT TCT AGC    1581
Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg Ile Ser Ser
                440                 445                 450

CTA CCA AAA TCA GAG AAG CCA TTA AAT GAG GAA ACA GTG GTA AAT AAG    1629
Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val Val Asn Lys
            455                 460                 465

AGA GAT GAA GAG CAG CAT CTT GAA TCT CAT ACA GAC TGC ATT CTT GCA    1677
Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys Ile Leu Ala
        470                 475                 480

GTA AAG CAG GCA ATA TCT GGA ACT TCT CCA GTG GCT TCT TCA TTT CAG    1725
Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser Ser Phe Gln
    485                 490                 495

GGT ATC AAA AAG TCT ATA TTC AGA ATA AGA GAA TCA CCT AAA GAG ACT    1773
Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro Lys Glu Thr
500                 505                 510                 515

TTC AAT GCA AGT TTT TCA GGT CAT ATG ACT GAT CCA AAC TTT AAA AAA    1821
Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn Phe Lys Lys
                520                 525                 530

GAA ACT GAA GCC TCT GAA AGT GGA CTG GAA ATA CAT ACT GTT TGC TCA    1869
Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr Val Cys Ser
            535                 540                 545

CAG AAG GAG GAC TCC TTA TGT CCA AAT TTA ATT GAT AAT GGA AGC TGG    1917
Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn Gly Ser Trp
        550                 555                 560

CCA GCC ACC ACC ACA CAG AAT TCT GTA GCT TTG AAG AAT GCA GGT TTA    1965
Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn Ala Gly Leu
    565                 570                 575

ATA TCC ACT TTG AAA AAG AAA ACA AAT AAG TTT ATT TAT GCT ATA CAT    2013
Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr Ala Ile His
580                 585                 590                 595

GAT GAA ACA TCT TAT AAA GGA AAA AAA ATA CCG AAA GAC CAA AAA TCA    2061
Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp Gln Lys Ser
                600                 605                 610

GAA CTA ATT AAC TGT TCA GCC CAG TTT GAA GCA AAT GCT TTT GAA GCA    2109
Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala Phe Glu Ala
            615                 620                 625

CCA CTT ACA TTT GCA AAT GCT GAT TCA GGT TTA TTG CAT TCT TCT GTG    2157
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Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His Ser Ser Val
        630                 635                 640

AAA AGA AGC TGT TCA CAG AAT GAT TCT GAA GAA CCA ACT TTG TCC TTA    2205
Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr Leu Ser Leu
    645                 650                 655

ACT AGC TCT TTT GGG ACA ATT CTG AGG AAA TGT TCT AGA AAT GAA ACA    2253
Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg Asn Glu Thr
660                 665                 670                 675

TGT TCT AAT AAT ACA GTA ATC TCT CAG GAT CTT GAT TAT AAA GAA GCA    2301
Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr Lys Glu Ala
                680                 685                 690

AAA TGT AAT AAG GAA AAA CTA CAG TTA TTT ATT ACC CCA GAA GCT GAT    2349
Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro Glu Ala Asp
            695                 700                 705

TCT CTG TCA TGC CTG CAG GAA GGA CAG TGT GAA AAT GAT CCA AAA AGC    2397
Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp Pro Lys Ser
        710                 715                 720

AAA AAA GTT TCA GAT ATA AAA GAA GAG GTC TTG GCT GCA GCA TGT CAC    2445
Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala Ala Cys His
    725                 730                 735

CCA GTA CAA CAT TCA AAA GTG GAA TAC AGT GAT ACT GAC TTT CAA TCC    2493
Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp Phe Gln Ser
740                 745                 750                 755

CAG AAA AGT CTT TTA TAT GAT CAT GAA AAT GCC AGC ACT CTT ATT TTA    2541
Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr Leu Ile Leu
                760                 765                 770

ACT CCT ACT TCC AAG GAT GTT CTG TCA AAC CTA GTC ATG ATT TCT AGA    2589
Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met Ile Ser Arg
            775                 780                 785

GGC AAA GAA TCA TAC AAA ATG TCA GAC AAG CTC AAA GGT AAC AAT TAT    2637
Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly Asn Asn Tyr
        790                 795                 800

GAA TCT GAT GTT GAA TTA ACC AAA AAT ATT CCC ATG GAA AAG AAT CAA    2685
Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu Lys Asn Gln
    805                 810                 815

GAT GTA TGT GCT TTA AAT GAA AAT TAT AAA AAC GTT GAG CTG TTG CCA    2733
Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu Leu Leu Pro
820                 825                 830                 835

CCT GAA AAA TAC ATG AGA GTA GCA TCA CCT TCA AGA AAG GTA CAA TTC    2781
Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys Val Gln Phe
                840                 845                 850

AAC CAA AAC ACA AAT CTA AGA GTA ATC CAA AAA AAT CAA GAA GAA ACT    2829
Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln Glu Glu Thr
            855                 860                 865

ACT TCA ATT TCA AAA ATA ACT GTC AAT CCA GAC TCT GAA GAA CTT TTC    2877
Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu Glu Leu Phe
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          870                 875                 880

     TCA GAC AAT GAG AAT AAT TTT GTC TTC CAA GTA GCT AAT GAA AGG AAT    2925
     Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn Glu Arg Asn
         885                 890                 895

     AAT CTT GCT TTA GGA AAT ACT AAG GAA CTT CAT GAA ACA GAC TTG ACT    2973
     Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr Asp Leu Thr
900                  905                 910                 915

     TGT GTA AAC GAA CCC ATT TTC AAG AAC TCT ACC ATG GTT TTA TAT GGA    3021
     Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val Leu Tyr Gly
                 920                 925                 930

     GAC ACA GGT GAT AAA CAA GCA ACC CAA GTG TCA ATT AAA AAA GAT TTG    3069
     Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys Lys Asp Leu
             935                 940                 945

     GTT TAT GTT CTT GCA GAG GAG AAC AAA AAT AGT GTA AAG CAG CAT ATA    3117
     Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys Gln His Ile
         950                 955                 960

     AAA ATG ACT CTA GGT CAA GAT TTA AAA TCG GAC ATC TCC TTG AAT ATA    3165
     Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser Leu Asn Ile
965                  970                 975

     GAT AAA ATA CCA GAA AAA AAT AAT GAT TAC ATG AAC AAA TGG GCA GGA    3213
     Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asn Lys Trp Ala Gly
980                  985                 990                 995

     CTC TTA GGT CCA ATT TCA AAT CAC AGT TTT GGA GGT AGC TTC AGA ACA    3261
     Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser Phe Arg Thr
                1000                1005                1010

     GCT TCA AAT AAG GAA ATC AAG CTC TCT GAA CAT AAC ATT AAG AAG AGC    3309
     Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile Lys Lys Ser
            1015                1020                1025

     AAA ATG TTC TTC AAA GAT ATT GAA GAA CAA TAT CCT ACT AGT TTA GCT    3357
     Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr Ser Leu Ala
        1030                1035                1040

     TGT GTT GAA ATT GTA AAT ACC TTG GCA TTA GAT AAT CAA AAG AAA CTG    3405
     Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln Lys Lys Leu
    1045                1050                1055

     AGC AAG CCT CAG TCA ATT AAT ACT GTA TCT GCA CAT TTA CAG AGT AGT    3453
     Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu Gln Ser Ser
1060                1065                1070                1075

     GTA GTT GTT TCT GAT TGT AAA AAT AGT CAT ATA ACC CCT CAG ATG TTA    3501
     Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro Gln Met Leu
                1080                1085                1090

     TTT TCC AAG CAG GAT TTT AAT TCA AAC CAT AAT TTA ACA CCT AGC CAA    3549
     Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr Pro Ser Gln
            1095                1100                1105

     AAG GCA GAA ATT ACA GAA CTT TCT ACT ATA TTA GAA GAA TCA GGA AGT    3597
     Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu Ser Gly Ser
        1110                1115                1120
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CAG TTT GAA TTT ACT CAG TTT AGA AAG CCA AGC TAC ATA TTG CAG AAG    3645
Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile Leu Gln Lys
   1125                1130                1135

AGT ACA TTT GAA GTG CCT GAA AAC CAG ATG ACT ATC TTA AAG ACC ACT    3693
Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu Lys Thr Thr
1140                1145                1150                1155

TCT GAG GAA TGC AGA GAT GCT GAT CTT CAT GTC ATA ATG AAT GCC CCA    3741
Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met Asn Ala Pro
                1160                1165                1170

TCG ATT GGT CAG GTA GAC AGC AGC AAG CAA TTT GAA GGT ACA GTT GAA    3789
Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly Thr Val Glu
            1175                1180                1185

ATT AAA CGG AAG TTT GCT GGC CTG TTG AAA AAT GAC TGT AAC AAA AGT    3837
Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys Asn Lys Ser
        1190                1195                1200

GCT TCT GGT TAT TTA ACA GAT GAA AAT GAA GTG GGG TTT AGG GGC TTT    3885
Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe Arg Gly Phe
   1205                1210                1215

TAT TCT GCT CAT GGC ACA AAA CTG AAT GTT TCT ACT GAA GCT CTG CAA    3933
Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu Ala Leu Gln
1220                1225                1230                1235

AAA GCT GTG AAA CTG TTT AGT GAT ATT GAG AAT ATT AGT GAG GAA ACT    3981
Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser Glu Glu Thr
                1240                1245                1250

TCT GCA GAG GTA CAT CCA ATA AGT TTA TCT TCA AGT AAA TGT CAT GAT    4029
Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys Cys His Asp
            1255                1260                1265

TCT GTT GTT TCA ATG TTT AAG ATA GAA AAT CAT AAT GAT AAA ACT GTA    4077
Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp Lys Thr Val
        1270                1275                1280

AGT GAA AAA AAT AAT AAA TGC CAA CTG ATA TTA CAA AAT AAT ATT GAA    4125
Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn Asn Ile Glu
   1285                1290                1295

ATG ACT ACT GGC ACT TTT GTT GAA GAA ATT ACT GAA AAT TAC AAG AGA    4173
Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn Tyr Lys Arg
1300                1305                1310                1315

AAT ACT GAA AAT GAA GAT AAC AAA TAT ACT GCT GCC AGT AGA AAT TCT    4221
Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser Arg Asn Ser
                1320                1325                1330

CAT AAC TTA GAA TTT GAT GGC AGT GAT TCA AGT AAA AAT GAT ACT GTT    4269
His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn Asp Thr Val
            1335                1340                1345

TGT ATT CAT AAA GAT GAA ACG GAC TTG CTA TTT ACT GAT CAG CAC AAC    4317
Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp Gln His Asn
        1350                1355                1360
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ATA TGT CTT AAA TTA TCT GGC CAG TTT ATG AAG GAG GGA AAC ACT CAG 4365
Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly Asn Thr Gln
1365 1370 1375

ATT AAA GAA GAT TTG TCA GAT TTA ACT TTT TTG GAA GTT GCG AAA GCT 4413
Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val Ala Lys Ala
1380 1385 1390 1395

CAA GAA GCA TGT CAT GGT AAT ACT TCA AAT AAA GAA CAG TTA ACT GCT 4461
Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln Leu Thr Ala
1400 1405 1410

ACT AAA ACG GAG CAA AAT ATA AAA GAT TTT GAG ACT TCT GAT ACA TTT 4509
Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser Asp Thr Phe
1415 1420 1425

TTT CAG ACT GCA AGT GGG AAA AAT ATT AGT GTC GCC AAA GAG TCA TTT 4557
Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys Glu Ser Phe
1430 1435 1440

AAT AAA ATT GTA AAT TTC TTT GAT CAG AAA CCA GAA GAA TTG CAT AAC 4605
Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu Leu His Asn
1445 1450 1455

TTT TCC TTA AAT TCT GAA TTA CAT TCT GAC ATA AGA AAG AAC AAA ATG 4653
Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys Asn Lys Met
1460 1465 1470 1475

GAC ATT CTA AGT TAT GAG GAA ACA GAC ATA GTT AAA CAC AAA ATA CTG 4701
Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His Lys Ile Leu
1480 1485 1490

AAA GAA AGT GTC CCA GTT GGT ACT GGA AAT CAA CTA GTG ACC TTC CAG 4749
Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val Thr Phe Gln
1495 1500 1505

GGA CAA CCC GAA CGT GAT GAA AAG ATC AAA GAA CCT ACT CTG TTG GGT 4797
Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr Leu Leu Gly
1510 1515 1520

TTT CAT ACA GCT AGC GGG AAA AAA GTT AAA ATT GCA AAG GAA TCT TTG 4845
Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys Glu Ser Leu
1525 1530 1535

GAC AAA GTG AAA AAC CTT TTT GAT GAA AAA GAG CAA GGT ACT AGT GAA 4893
Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly Thr Ser Glu
1540 1545 1550 1555

ATC ACC AGT TTT AGC CAT CAA TGG GCA AAG ACC CTA AAG TAC AGA GAG 4941
Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys Tyr Arg Glu
1560 1565 1570

GCC TGT AAA GAC CTT GAA TTA GCA TGT GAG ACC ATT GAG ATC ACA GCT 4989
Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu Ile Thr Ala
1575 1580 1585

GCC CCA AAG TGT AAA GAA ATG CAG AAT TCT CTC AAT AAT GAT AAA AAC 5037
Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn Asp Lys Asn
1590 1595 1600

CTT GTT TCT ATT GAG ACT GTG GTG CCA CCT AAG CTC TTA AGT GAT AAT 5085

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Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu Ser Asp Asn
   1605                1610                1615

TTA TGT AGA CAA ACT GAA AAT CTC AAA ACA TCA AAA AGT ATC TTT TTG    5133
Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser Ile Phe Leu
1620                1625                1630                1635

AAA GTT AAA GTA CAT GAA AAT GTA GAA AAA GAA ACA GCA AAA AGT CCT    5181
Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala Lys Ser Pro
                1640                1645                1650

GCA ACT TGT TAC ACA AAT CAG TCC CCT TAT TCA GTC ATT GAA AAT TCA    5229
Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile Glu Asn Ser
            1655                1660                1665

GCC TTA GCT TTT TAC ACA AGT TGT AGT AGA AAA ACT TCT GTG AGT CAG    5277
Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser Val Ser Gln
        1670                1675                1680

ACT TCA TTA CTT GAA GCA AAA AAA TGG CTT AGA GAA GGA ATA TTT GAT    5325
Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly Ile Phe Asp
    1685                1690                1695

GGT CAA CCA GAA AGA ATA AAT ACT GCA GAT TAT GTA GGA AAT TAT TTG    5373
Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly Asn Tyr Leu
1700                1705                1710                1715

TAT GAA AAT AAT TCA AAC AGT ACT ATA GCT GAA AAT GAC AAA AAT CAT    5421
Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp Lys Asn His
                1720                1725                1730

CTC TCC GAA AAA CAA GAT ACT TAT TTA AGT AAC AGT AGC ATG TCT AAC    5469
Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser Met Ser Asn
            1735                1740                1745

AGC TAT TCC TAC CAT TCT GAT GAG GTA TAT AAT GAT TCA GGA TAT CTC    5517
Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser Gly Tyr Leu
        1750                1755                1760

TCA AAA AAT AAA CTT GAT TCT GGT ATT GAG CCA GTA TTG AAG AAT GTT    5565
Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu Lys Asn Val
    1765                1770                1775

GAA GAT CAA AAA AAC ACT AGT TTT TCC AAA GTA ATA TCC AAT GTA AAA    5613
Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser Asn Val Lys
1780                1785                1790                1795

GAT GCA AAT GCA TAC CCA CAA ACT GTA AAT GAA GAT ATT TGC GTT GAG    5661
Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile Cys Val Glu
                1800                1805                1810

GAA CTT GTG ACT AGC TCT TCA CCC TGC AAA AAT AAA AAT GCA GCC ATT    5709
Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn Ala Ala Ile
            1815                1820                1825

AAA TTG TCC ATA TCT AAT AGT AAT AAT TTT GAG GTA GGG CCA CCT GCA    5757
Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly Pro Pro Ala
        1830                1835                1840

TTT AGG ATA GCC AGT GGT AAA ATC GTT TGT GTT TCA CAT GAA ACA ATT    5805
Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His Glu Thr Ile
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          1845                1850                1855

      AAA AAA GTG AAA GAC ATA TTT ACA GAC AGT TTC AGT AAA GTA ATT AAG    5853
 5    Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys Val Ile Lys
     1860                1865                1870                1875

      GAA AAC AAC GAG AAT AAA TCA AAA ATT TGC CAA ACG AAA ATT ATG GCA    5901
      Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys Ile Met Ala
10                 1880                1885                1890

      GGT TGT TAC GAG GCA TTG GAT GAT TCA GAG GAT ATT CTT CAT AAC TCT    5949
      Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu His Asn Ser
            1895                1900                1905
15
      CTA GAT AAT GAT GAA TGT AGC ACG CAT TCA CAT AAG GTT TTT GCT GAC    5997
      Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val Phe Ala Asp
         1910                1915                1920

20    ATT CAG AGT GAA GAA ATT TTA CAA CAT AAC CAA AAT ATG TCT GGA TTG    6045
      Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met Ser Gly Leu
         1925                1930                1935

      GAG AAA GTT TCT AAA ATA TCA CCT TGT GAT GTT AGT TTG GAA ACT TCA    6093
25    Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu Glu Thr Ser
     1940                1945                1950                1955

      GAT ATA TGT AAA TGT AGT ATA GGG AAG CTT CAT AAG TCA GTC TCA TCT    6141
      Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser Val Ser Ser
30                 1960                1965                1970

      GCA AAT ACT TGT GGG ATT TTT AGC ACA GCA AGT GGA AAA TCT GTC CAG    6189
      Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys Ser Val Gln
            1975                1980                1985
35
      GTA TCA GAT GCT TCA TTA CAA AAC GCA AGA CAA GTG TTT TCT GAA ATA    6237
      Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe Ser Glu Ile
         1990                1995                2000

40    GAA GAT AGT ACC AAG CAA GTC TTT TCC AAA GTA TTG TTT AAA AGT AAC    6285
      Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe Lys Ser Asn
         2005                2010                2015

      GAA CAT TCA GAC CAG CTC ACA AGA GAA GAA AAT ACT GCT ATA CGT ACT    6333
45    Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala Ile Arg Thr
     2020                2025                2030                2035

      CCA GAA CAT TTA ATA TCC CAA AAA GGC TTT TCA TAT AAT GTG GTA AAT    6381
      Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn Val Val Asn
50                 2040                2045                2050

      TCA TCT GCT TTC TCT GGA TTT AGT ACA GCA AGT GGA AAG CAA GTT TCC    6429
      Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys Gln Val Ser
            2055                2060                2065
55
      ATT TTA GAA AGT TCC TTA CAC AAA GTT AAG GGA GTG TTA GAG GAA TTT    6477
      Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu Glu Glu Phe
         2070                2075                2080

60    GAT TTA ATC AGA ACT GAG CAT AGT CTT CAC TAT TCA CCT ACG TCT AGA    6525
      Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro Thr Ser Arg
         2085                2090                2095
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CAA AAT GTA TCA AAA ATA CTT CCT CGT GTT GAT AAG AGA AAC CCA GAG    6573
Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg Asn Pro Glu
2100                2105                2110                2115

CAC TGT GTA AAC TCA GAA ATG GAA AAA ACC TGC AGT AAA GAA TTT AAA    6621
His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys Glu Phe Lys
                2120                2125                2130

TTA TCA AAT AAC TTA AAT GTT GAA GGT GGT TCT TCA GAA AAT AAT CAC    6669
Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu Asn Asn His
            2135                2140                2145

TCT ATT AAA GTT TCT CCA TAT CTC TCT CAA TTT CAA CAA GAC AAA CAA    6717
Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln Asp Lys Gln
        2150                2155                2160

CAG TTG GTA TTA GGA ACC AAA GTC TCA CTT GTT GAG AAC ATT CAT GTT    6765
Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn Ile His Val
    2165                2170                2175

TTG GGA AAA GAA CAG GCT TCA CCT AAA AAC GTA AAA ATG GAA ATT GGT    6813
Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met Glu Ile Gly
2180                2185                2190                2195

AAA ACT GAA ACT TTT TCT GAT GTT CCT GTG AAA ACA AAT ATA GAA GTT    6861
Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn Ile Glu Val
                2200                2205                2210

TGT TCT ACT TAC TCC AAA GAT TCA GAA AAC TAC TTT GAA ACA GAA GCA    6909
Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu Thr Glu Ala
            2215                2220                2225

GTA GAA ATT GCT AAA GCT TTT ATG GAA GAT GAT GAA CTG ACA GAT TCT    6957
Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu Thr Asp Ser
        2230                2235                2240

AAA CTG CCA AGT CAT GCC ACA CAT TCT CTT TTT ACA TGT CCC GAA AAT    7005
Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys Pro Glu Asn
    2245                2250                2255

GAG GAA ATG GTT TTG TCA AAT TCA AGA ATT GGA AAA AGA AGA GGA GAG    7053
Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg Arg Gly Glu
2260                2265                2270                2275

CCC CTT ATC TTA GTG GGA GAA CCC TCA ATC AAA AGA AAC TTA TTA AAT    7101
Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn Leu Leu Asn
                2280                2285                2290

GAA TTT GAC AGG ATA ATA GAA AAT CAA GAA AAA TCC TTA AAG GCT TCA    7149
Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu Lys Ala Ser
            2295                2300                2305

AAA AGC ACT CCA GAT GGC ACA ATA AAA GAT CGA AGA TTG TTT ATG CAT    7197
Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu Phe Met His
        2310                2315                2320

CAT GTT TCT TTA GAG CCG ATT ACC TGT GTA CCC TTT CGC ACA ACT AAG    7245
His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg Thr Thr Lys
    2325                2330                2335
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GAA CGT CAA GAG ATA CAG AAT CCA AAT TTT ACC GCA CCT GGT CAA GAA 7293
Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro Gly Gln Glu
2340 2345 2350 2355

TTT CTG TCT AAA TCT CAT TTG TAT GAA CAT CTG ACT TTG GAA AAA TCT 7341
Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu Glu Lys Ser
2360 2365 2370

TCA AGC AAT TTA GCA GTT TCA GGA CAT CCA TTT TAT CAA GTT TCT GCT 7389
Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln Val Ser Ala
2375 2380 2385

ACA AGA AAT GAA AAA ATG AGA CAC TTG ATT ACT ACA GGC AGA CCA ACC 7437
Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly Arg Pro Thr
2390 2395 2400

AAA GTC TTT GTT CCA CCT TTT AAA ACT AAA TCG CAT TTT CAC AGA GTT 7485
Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe His Arg Val
2405 2410 2415

GAA CAG TGT GTT AGG AAT ATT AAC TTG GAG GAA AAC AGA CAA AAG CAA 7533
Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg Gln Lys Gln
2420 2425 2430 2435

AAC ATT GAT GGA CAT GGC TCT GAT GAT AGT AAA AAT AAG ATT AAT GAC 7581
Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys Ile Asn Asp
2440 2445 2450

AAT GAG ATT CAT CAG TTT AAC AAA AAC AAC TCC AAT CAA GCA GCA GCT 7629
Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln Ala Ala Ala
2455 2460 2465

GTA ACT TTC ACA AAG TGT GAA GAA GAA CCT TTA GAT TTA ATT ACA AGT 7677
Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu Ile Thr Ser
2470 2475 2480

CTT CAG AAT GCC AGA GAT ATA CAG GAT ATG CGA ATT AAG AAG AAA CAA 7725
Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys Lys Lys Gln
2485 2490 2495

AGG CAA CGC GTC TTT CCA CAG CCA GGC AGT CTG TAT CTT GCA AAA ACA 7773
Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu Ala Lys Thr
2500 2505 2510 2515

TCC ACT CTG CCT CGA ATC TCT CTG AAA GCA GCA GTA GGA GGC CAA GTT 7821
Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly Gly Gln Val
2520 2525 2530

CCC TCT GCG TGT TCT CAT AAA CAG CTG TAT ACG TAT GGC GTT TCT AAA 7869
Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly Val Ser Lys
2535 2540 2545

CAT TGC ATA AAA ATT AAC AGC AAA AAT GCA GAG TCT TTT CAG TTT CAC 7917
His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe Gln Phe His
2550 2555 2560

ACT GAA GAT TAT TTT GGT AAG GAA AGT TTA TGG ACT GGA AAA GGA ATA 7965
Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly Lys Gly Ile
2565 2570 2575

CAG TTG GCT GAT GGT GGA TGG CTC ATA CCC TCC AAT GAT GGA AAG GCT 8013

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      Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp Gly Lys Ala
     2580                2585                2590                2595

 5   GGA AAA GAA GAA TTT TAT AGG GCT CTG TGT GAC ACT CCA GGT GTG GAT    8061
     Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro Gly Val Asp
                    2600                2605                2610

     CCA AAG CTT ATT TCT AGA ATT TGG GTT TAT AAT CAC TAT AGA TGG ATC    8109
10   Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr Arg Trp Ile
               2615                2620                2625

     ATA TGG AAA CTG GCA GCT ATG GAA TGT GCC TTT CCT AAG GAA TTT GCT    8157
     Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys Glu Phe Ala
15         2630                2635                2640

     AAT AGA TGC CTA AGC CCA GAA AGG GTG CTT CTT CAA CTA AAA TAC AGA    8205
     Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu Lys Tyr Arg
        2645                2650                2655
20
     TAT GAT ACG GAA ATT GAT AGA AGC AGA AGA TCG GCT ATA AAA AAG ATA    8253
     Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile Lys Lys Ile
     2660                2665                2670                2675

25   ATG GAA AGG GAT GAC ACA GCT GCA AAA ACA CTT GTT CTC TGT GTT TCT    8301
     Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu Cys Val Ser
                    2680                2685                2690

     GAC ATA ATT TCA TTG AGC GCA AAT ATA TCT GAA ACT TCT AGC AAT AAA    8349
30   Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser Ser Asn Lys
               2695                2700                2705

     ACT AGT AGT GCA GAT ACC CAA AAA GTG GCC ATT ATT GAA CTT ACA GAT    8397
     Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu Leu Thr Asp
35         2710                2715                2720

     GGG TGG TAT GCT GTT AAG GCC CAG TTA GAT CCT CCC CTC TTA GCT GTC    8445
     Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu Leu Ala Val
        2725                2730                2735
40
     TTA AAG AAT GGC AGA CTG ACA GTT GGT CAG AAG ATT ATT CTT CAT GGA    8493
     Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile Leu His Gly
     2740                2745                2750                2755

45   GCA GAA CTG GTG GGC TCT CCT GAT GCC TGT ACA CCT CTT GAA GCC CCA    8541
     Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu Glu Ala Pro
                    2760                2765                2770

     GAA TCT CTT ATG TTA AAG ATT TCT GCT AAC AGT ACT CGG CCT GCT CGC    8589
50   Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg Pro Ala Arg
               2775                2780                2785

     TGG TAT ACC AAA CTT GGA TTC TTT CCT GAC CCT AGA CCT TTT CCT CTG    8637
     Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro Phe Pro Leu
55         2790                2795                2800

     CCC TTA TCA TCG CTT TTC AGT GAT GGA GGA AAT GTT GGT TGT GTT GAT    8685
     Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly Cys Val Asp
        2805                2810                2815
60
     GTA ATT ATT CAA AGA GCA TAC CCT ATA CAG TGG ATG GAG AAG ACA TCA    8733
     Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu Lys Thr Ser
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2820                2825                2830                2835

TCT GGA TTA TAC ATA TTT CGC AAT GAA AGA GAG GAA GAA AAG GAA GCA    8781
Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu Lys Glu Ala
                2840                2845                2850

GCA AAA TAT GTG GAG GCC CAA CAA AAG AGA CTA GAA GCC TTA TTC ACT    8829
Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala Leu Phe Thr
            2855                2860                2865

AAA ATT CAG GAG GAA TTT GAA GAA CAT GAA GAA AAC ACA ACA AAA CCA    8877
Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr Thr Lys Pro
        2870                2875                2880

TAT TTA CCA TCA CGT GCA CTA ACA AGA CAG CAA GTT CGT GCT TTG CAA    8925
Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg Ala Leu Gln
    2885                2890                2895

GAT GGT GCA GAG CTT TAT GAA GCA GTG AAG AAT GCA GCA GAC CCA GCT    8973
Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala Asp Pro Ala
2900                2905                2910                2915

TAC CTT GAG GGT TAT TTC AGT GAA GAG CAG TTA AGA GCC TTG AAT AAT    9021
Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala Leu Asn Asn
                2920                2925                2930

CAC AGG CAA ATG TTG AAT GAT AAG AAA CAA GCT CAG ATC CAG TTG GAA    9069
His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile Gln Leu Glu
            2935                2940                2945

ATT AGG AAG GCC ATG GAA TCT GCT GAA CAA AAG GAA CAA GGT TTA TCA    9117
Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln Gly Leu Ser
        2950                2955                2960

AGG GAT GTC ACA ACC GTG TGG AAG TTG CGT ATT GTA AGC TAT TCA AAA    9165
Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser Tyr Ser Lys
    2965                2970                2975

AAA GAA AAA GAT TCA GTT ATA CTG AGT ATT TGG CGT CCA TCA TCA GAT    9213
Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro Ser Ser Asp
2980                2985                2990                2995

TTA TAT TCT CTG TTA ACA GAA GGA AAG AGA TAC AGA ATT TAT CAT CTT    9261
Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile Tyr His Leu
                3000                3005                3010

GCA ACT TCA AAA TCT AAA AGT AAA TCT GAA AGA GCT AAC ATA CAG TTA    9309
Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn Ile Gln Leu
            3015                3020                3025

GCA GCG ACA AAA AAA ACT CAG TAT CAA CAA CTA CCG GTT TCA GAT GAA    9357
Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val Ser Asp Glu
        3030                3035                3040

ATT TTA TTT CAG ATT TAC CAG CCA CGG GAG CCC CTT CAC TTC AGC AAA    9405
Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His Phe Ser Lys
    3045                3050                3055

TTT TTA GAT CCA GAC TTT CAG CCA TCT TGT TCT GAG GTG GAC CTA ATA    9453
Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val Asp Leu Ile
3060                3065                3070                3075
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GGA TTT GTC GTT TCT GTT GTG AAA AAA ACA GGA CTT GCC CCT TTC GTC 9501
Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala Pro Phe Val
3080 3085 3090

TAT TTG TCA GAC GAA TGT TAC AAT TTA CTG GCA ATA AAG TTT TGG ATA 9549
Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys Phe Trp Ile
3095 3100 3105

GAC CTT AAT GAG GAC ATT ATT AAG CCT CAT ATG TTA ATT GCT GCA AGC 9597
Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile Ala Ala Ser
3110 3115 3120

AAC CTC CAG TGG CGA CCA GAA TCC AAA TCA GGC CTT CTT ACT TTA TTT 9645
Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu Thr Leu Phe
3125 3130 3135

GCT GGA GAT TTT TCT GTG TTT TCT GCT AGT CCA AAA GAG GGC CAC TTT 9693
Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu Gly His Phe
3140 3145 3150 3155

CAA GAG ACA TTC AAC AAA ATG AAA AAT ACT GTT GAG AAT ATT GAC ATA 9741
Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn Ile Asp Ile
3160 3165 3170

CTT TGC AAT GAA GCA GAA AAC AAG CTT ATG CAT ATA CTG CAT GCA AAT 9789
Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu His Ala Asn
3175 3180 3185

GAT CCC AAG TGG TCC ACC CCA ACT AAA GAC TGT ACT TCA GGG CCG TAC 9837
Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser Gly Pro Tyr
3190 3195 3200

ACT GCT CAA ATC ATT CCT GGT ACA GGA AAC AAG CTT CTG ATG TCT TCT 9885
Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu Met Ser Ser
3205 3210 3215

CCT AAT TGT GAG ATA TAT TAT CAA AGT CCT TTA TCA CTT TGT ATG GCC 9933
Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu Cys Met Ala
3220 3225 3230 3235

AAA AGG AAG TCT GTT TCC ACA CCT GTC TCA GCC CAG ATG ACT TCA AAG 9981
Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met Thr Ser Lys
3240 3245 3250

TCT TGT AAA GGG GAG AAA GAG ATT GAT GAC CAA AAG AAC TGC AAA AAG 10029
Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn Cys Lys Lys
3255 3260 3265

AGA AGA GCC TTG GAT TTC TTG AGT AGA CTG CCT TTA CCT CCA CCT GTT 10077
Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro Pro Pro Val
3270 3275 3280

AGT CCC ATT TGT ACA TTT GTT TCT CCG GCT GCA CAG AAG GCA TTT CAG 10125
Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys Ala Phe Gln
3285 3290 3295

CCA CCA AGG AGT TGT GGC ACC AAA TAC GAA ACA CCC ATA AAG AAA AAA 10173
Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile Lys Lys Lys
3300 3305 3310 3315

GAA CTG AAT TCT CCT CAG ATG ACT CCA TTT AAA AAA TTC AAT GAA ATT 10221
Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe Asn Glu Ile
3320 3325 3330

TCT CTT TTG GAA AGT AAT TCA ATA GCT GAC GAA GAA CTT GCA TTG ATA 10269
Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile
3335 3340 3345

AAT ACC CAA GCT CTT TTG TCT GGT TCA ACA GGA GAA AAA CAA TTT ATA 10317
Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys Gln Phe Ile
3350 3355 3360

TCT GTC AGT GAA TCC ACT AGG ACT GCT CCC ACC AGT TCA GAA GAT TAT 10365
Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp Tyr
3365 3370 3375

CTC AGA CTG AAA CGA CGT TGT ACT ACA TCT CTG ATC AAA GAA CAG GAG 10413
Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu Gln Glu
3380 3385 3390 3395

AGT TCC CAG GCC AGT ACG GAA GAA TGT GAG AAA AAT AAG CAG GAC ACA 10461
Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys Gln Asp Thr
3400 3405 3410

ATT ACA ACT AAA AAA TAT ATC TAA 10485
Ile Thr Thr Lys Lys Tyr Ile
3415

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3418 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Met Pro Ile Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys
1 5 10 15
Thr Arg Cys Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe
20 25 30
Glu Glu Leu Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu
35 40 45
Glu Ser Glu His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr
50 55 60
Pro Gln Arg Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile
65 70 75 80
Phe Lys Glu Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys
85 90 95
Glu Leu Asp Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser
100 105 110
Arg His Lys Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp
115 120 125
Asp Val Ser Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val
130 135 140
Val Leu Gln Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val

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145                 150                 155                 160
Cys Gly Ser Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr
                165                 170                 175
Pro Lys His Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met
            180                 185                 190
Ser Trp Ser Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val
        195                 200                 205
Leu Ile Val Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp
    210                 215                 220
Thr Thr Ala Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu
225                 230                 235                 240
Lys Lys Asn Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr
                245                 250                 255
Asn Gln Arg Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn
            260                 265                 270
Ser Phe Lys Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro
        275                 280                 285
Asn Val Leu Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu
    290                 295                 300
Glu Asp Ser Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu
305                 310                 315                 320
Gln Lys Val Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala
                325                 330                 335
Asn Ala Asp Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr
            340                 345                 350
Ser Phe Val Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser
        355                 360                 365
Asn Val Ala His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser
    370                 375                 380
Lys Glu Val Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu
385                 390                 395                 400
Ser Gly Leu Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile
                405                 410                 415
Ser Ser Cys Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu
            420                 425                 430
Asn Lys Arg Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg
        435                 440                 445
Ile Ser Ser Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val
    450                 455                 460
Val Asn Lys Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys
465                 470                 475                 480
Ile Leu Ala Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser
                485                 490                 495
Ser Phe Gln Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro
            500                 505                 510
Lys Glu Thr Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn
        515                 520                 525
Phe Lys Lys Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr
    530                 535                 540
Val Cys Ser Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn
545                 550                 555                 560
Gly Ser Trp Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn
                565                 570                 575
Ala Gly Leu Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr
            580                 585                 590
Ala Ile His Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp
        595                 600                 605
Gln Lys Ser Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala
    610                 615                 620
Phe Glu Ala Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His
625                 630                 635                 640
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Ser Ser Val Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr
645 650 655
Leu Ser Leu Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg
660 665 670
Asn Glu Thr Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr
675 680 685
Lys Glu Ala Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro
690 695 700
Glu Ala Asp Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp
705 710 715 720
Pro Lys Ser Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala
725 730 735
Ala Cys His Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp
740 745 750
Phe Gln Ser Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr
755 760 765
Leu Ile Leu Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met
770 775 780
Ile Ser Arg Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly
785 790 795 800
Asn Asn Tyr Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu
805 810 815
Lys Asn Gln Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu
820 825 830
Leu Leu Pro Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys
835 840 845
Val Gln Phe Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln
850 855 860
Glu Glu Thr Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu
865 870 875 880
Glu Leu Phe Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn
885 890 895
Glu Arg Asn Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr
900 905 910
Asp Leu Thr Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val
915 920 925
Leu Tyr Gly Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys
930 935 940
Lys Asp Leu Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys
945 950 955 960
Gln His Ile Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser
965 970 975
Leu Asn Ile Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asn Lys
980 985 990
Trp Ala Gly Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser
995 1000 1005
Phe Arg Thr Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile
1010 1015 1020
Lys Lys Ser Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr
1025 1030 1035 104
Ser Leu Ala Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln
1045 1050 1055
Lys Lys Leu Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu
1060 1065 1070
Gln Ser Ser Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro
1075 1080 1085
Gln Met Leu Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr
1090 1095 1100
Pro Ser Gln Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu
1105 1110 1115 112
Ser Gly Ser Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile

1125 1130 1135
Leu Gln Lys Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu
1140 1145 1150
Lys Thr Thr Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met
1155 1160 1165
Asn Ala Pro Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly
1170 1175 1180
Thr Val Glu Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys
1185 1190 1195 120
Asn Lys Ser Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe
1205 1210 1215
Arg Gly Phe Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu
1220 1225 1230
Ala Leu Gln Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser
1235 1240 1245
Glu Glu Thr Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys
1250 1255 1260
Cys His Asp Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp
1265 1270 1275 128
Lys Thr Val Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn
1285 1290 1295
Asn Ile Glu Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn
1300 1305 1310
Tyr Lys Arg Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser
1315 1320 1325
Arg Asn Ser His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn
1330 1335 1340
Asp Thr Val Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp
1345 1350 1355 136
Gln His Asn Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly
1365 1370 1375
Asn Thr Gln Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val
1380 1385 1390
Ala Lys Ala Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln
1395 1400 1405
Leu Thr Ala Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser
1410 1415 1420
Asp Thr Phe Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys
1425 1430 1435 144
Glu Ser Phe Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu
1445 1450 1455
Leu His Asn Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys
1460 1465 1470
Asn Lys Met Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His
1475 1480 1485
Lys Ile Leu Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val
1490 1495 1500
Thr Phe Gln Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr
1505 1510 1515 152
Leu Leu Gly Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys
1525 1530 1535
Glu Ser Leu Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly
1540 1545 1550
Thr Ser Glu Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys
1555 1560 1565
Tyr Arg Glu Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu
1570 1575 1580
Ile Thr Ala Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn
1585 1590 1595 160
Asp Lys Asn Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu
1605 1610 1615

Ser Asp Asn Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser
1620 1625 1630
Ile Phe Leu Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala
1635 1640 1645
Lys Ser Pro Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile
1650 1655 1660
Glu Asn Ser Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser
1665 1670 1675 168
Val Ser Gln Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly
1685 1690 1695
Ile Phe Asp Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly
1700 1705 1710
Asn Tyr Leu Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp
1715 1720 1725
Lys Asn His Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser
1730 1735 1740
Met Ser Asn Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser
1745 1750 1755 176
Gly Tyr Leu Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu
1765 1770 1775
Lys Asn Val Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser
1780 1785 1790
Asn Val Lys Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile
1795 1800 1805
Cys Val Glu Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn
1810 1815 1820
Ala Ala Ile Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly
1825 1830 1835 184
Pro Pro Ala Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His
1845 1850 1855
Glu Thr Ile Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys
1860 1865 1870
Val Ile Lys Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys
1875 1880 1885
Ile Met Ala Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu
1890 1895 1900
His Asn Ser Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val
1905 1910 1915 192
Phe Ala Asp Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met
1925 1930 1935
Ser Gly Leu Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu
1940 1945 1950
Glu Thr Ser Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser
1955 1960 1965
Val Ser Ser Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys
1970 1975 1980
Ser Val Gln Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe
1985 1990 1995 200
Ser Glu Ile Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe
2005 2010 2015
Lys Ser Asn Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala
2020 2025 2030
Ile Arg Thr Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn
2035 2040 2045
Val Val Asn Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys
2050 2055 2060
Gln Val Ser Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu
2065 2070 2075 208
Glu Glu Phe Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro
2085 2090 2095
Thr Ser Arg Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg

2100 2105 2110
Asn Pro Glu His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys
2115 2120 2125
Glu Phe Lys Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu
2130 2135 2140
Asn Asn His Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln
2145 2150 2155 216
Asp Lys Gln Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn
2165 2170 2175
Ile His Val Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met
2180 2185 2190
Glu Ile Gly Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn
2195 2200 2205
Ile Glu Val Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu
2210 2215 2220
Thr Glu Ala Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu
2225 2230 2235 224
Thr Asp Ser Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys
2245 2250 2255
Pro Glu Asn Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg
2260 2265 2270
Arg Gly Glu Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn
2275 2280 2285
Leu Leu Asn Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu
2290 2295 2300
Lys Ala Ser Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu
2305 2310 2315 232
Phe Met His His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg
2325 2330 2335
Thr Thr Lys Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro
2340 2345 2350
Gly Gln Glu Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu
2355 2360 2365
Glu Lys Ser Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln
2370 2375 2380
Val Ser Ala Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly
2385 2390 2395 240
Arg Pro Thr Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe
2405 2410 2415
His Arg Val Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg
2420 2425 2430
Gln Lys Gln Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys
2435 2440 2445
Ile Asn Asp Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln
2450 2455 2460
Ala Ala Ala Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu
2465 2470 2475 248
Ile Thr Ser Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys
2485 2490 2495
Lys Lys Gln Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu
2500 2505 2510
Ala Lys Thr Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly
2515 2520 2525
Gly Gln Val Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly
2530 2535 2540
Val Ser Lys His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe
2545 2550 2555 256
Gln Phe His Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly
2565 2570 2575
Lys Gly Ile Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp
2580 2585 2590

Gly Lys Ala Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro
2595 2600 2605
Gly Val Asp Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr
2610 2615 2620
Arg Trp Ile Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys
2625 2630 2635 264
Glu Phe Ala Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu
2645 2650 2655
Lys Tyr Arg Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile
2660 2665 2670
Lys Lys Ile Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu
2675 2680 2685
Cys Val Ser Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser
2690 2695 2700
Ser Asn Lys Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu
2705 2710 2715 272
Leu Thr Asp Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu
2725 2730 2735
Leu Ala Val Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile
2740 2745 2750
Leu His Gly Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu
2755 2760 2765
Glu Ala Pro Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg
2770 2775 2780
Pro Ala Arg Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro
2785 2790 2795 280
Phe Pro Leu Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly
2805 2810 2815
Cys Val Asp Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu
2820 2825 2830
Lys Thr Ser Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu
2835 2840 2845
Lys Glu Ala Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala
2850 2855 2860
Leu Phe Thr Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr
2865 2870 2875 288
Thr Lys Pro Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg
2885 2890 2895
Ala Leu Gln Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala
2900 2905 2910
Asp Pro Ala Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala
2915 2920 2925
Leu Asn Asn His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile
2930 2935 2940
Gln Leu Glu Ile Arg Lys Ala Met Glu Ser Ala Glu Gln Lys Glu Gln
2945 2950 2955 296
Gly Leu Ser Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser
2965 2970 2975
Tyr Ser Lys Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro
2980 2985 2990
Ser Ser Asp Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile
2995 3000 3005
Tyr His Leu Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn
3010 3015 3020
Ile Gln Leu Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val
3025 3030 3035 304
Ser Asp Glu Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His
3045 3050 3055
Phe Ser Lys Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val
3060 3065 3070
Asp Leu Ile Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala

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        3075                3080                3085
Pro Phe Val Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys
    3090                3095                3100
Phe Trp Ile Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile
3105                3110                3115                312
Ala Ala Ser Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu
                3125                3130                3135
Thr Leu Phe Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu
            3140                3145                3150
Gly His Phe Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn
        3155                3160                3165
Ile Asp Ile Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu
    3170                3175                3180
His Ala Asn Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser
3185                3190                3195                320
Gly Pro Tyr Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu
                3205                3210                3215
Met Ser Ser Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu
            3220                3225                3230
Cys Met Ala Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met
        3235                3240                3245
Thr Ser Lys Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn
    3250                3255                3260
Cys Lys Lys Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro
3265                3270                3275                328
Pro Pro Val Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys
                3285                3290                3295
Ala Phe Gln Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile
            3300                3305                3310
Lys Lys Lys Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe
        3315                3320                3325
Asn Glu Ile Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu
    3330                3335                3340
Ala Leu Ile Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys
3345                3350                3355                336
Gln Phe Ile Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser
                3365                3370                3375
Glu Asp Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys
            3380                3385                3390
Glu Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys
        3395                3400                3405
Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile
    3410                3415
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(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10485 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 229...10482
(D) OTHER INFORMATION: BRCA2 (OMI5)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

GGTGGCGCGA GCTTCTGAAA CTAGGCGGCA GAGGCGGAGC CGCTGTGGCA CTGCTGCGCC 60
TCTGCTGCGC CTCGGGTGTC TTTTGCGGCG GTGGGTCGCC GCCGGGAGAA GCGTGAGGGG 120
ACAGATTTGT GACCGGCGCG GTTTTTGTCA GCTTACTCCG GCCAAAAAAG AACTGCACCT 180
CTGGAGCGGA CTTATTTACC AAGCATTGGA GGAATATCGT AGGTAAAA ATG CCT ATT 237
Met Pro Ile
1

GGA TCC AAA GAG AGG CCA ACA TTT TTT GAA ATT TTT AAG ACA CGC TGC 285
Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys Thr Arg Cys
5 10 15

AAC AAA GCA GAT TTA GGA CCA ATA AGT CTT AAT TGG TTT GAA GAA CTT 333
Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe Glu Glu Leu
20 25 30 35

TCT TCA GAA GCT CCA CCC TAT AAT TCT GAA CCT GCA GAA GAA TCT GAA 381
Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu Glu Ser Glu
40 45 50

CAT AAA AAC AAC AAT TAC GAA CCA AAC CTA TTT AAA ACT CCA CAA AGG 429
His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr Pro Gln Arg
55 60 65

AAA CCA TCT TAT AAT CAG CTG GCT TCA ACT CCA ATA ATA TTC AAA GAG 477
Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile Phe Lys Glu
70 75 80

CAA GGG CTG ACT CTG CCG CTG TAC CAA TCT CCT GTA AAA GAA TTA GAT 525
Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys Glu Leu Asp
85 90 95

AAA TTC AAA TTA GAC TTA GGA AGG AAT GTT CCC AAT AGT AGA CAT AAA 573
Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser Arg His Lys
100 105 110 115

AGT CTT CGC ACA GTG AAA ACT AAA ATG GAT CAA GCA GAT GAT GTT TCC 621
Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp Asp Val Ser
120 125 130

TGT CCA CTT CTA AAT TCT TGT CTT AGT GAA AGT CCT GTT GTT CTA CAA 669
Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val Val Leu Gln
135 140 145

TGT ACA CAT GTA ACA CCA CAA AGA GAT AAG TCA GTG GTA TGT GGG AGT 717
Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val Cys Gly Ser
150 155 160

TTG TTT CAT ACA CCA AAG TTT GTG AAG GGT CGT CAG ACA CCA AAA CAT 765
Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr Pro Lys His
165 170 175

ATT TCT GAA AGT CTA GGA GCT GAG GTG GAT CCT GAT ATG TCT TGG TCA 813
Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met Ser Trp Ser
180 185 190 195

AGT TCT TTA GCT ACA CCA CCC ACC CTT AGT TCT ACT GTG CTC ATA GTC 861
Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val Leu Ile Val
200 205 210

AGA AAT GAA GAA GCA TCT GAA ACT GTA TTT CCT CAT GAT ACT ACT GCT 909
Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp Thr Thr Ala

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                215                 220                 225

     AAT GTG AAA AGC TAT TTT TCC AAT CAT GAT GAA AGT CTG AAG AAA AAT     957
 5   Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu Lys Lys Asn
         230                 235                 240

     GAT AGA TTT ATC GCT TCT GTG ACA GAC AGT GAA AAC ACA AAT CAA AGA    1005
     Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr Asn Gln Arg
10       245                 250                 255

     GAA GCT GCA AGT CAT GGA TTT GGA AAA ACA TCA GGG AAT TCA TTT AAA    1053
     Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn Ser Phe Lys
     260                 265                 270                 275
15
     GTA AAT AGC TGC AAA GAC CAC ATT GGA AAG TCA ATG CCA CAT GTC CTA    1101
     Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro His Val Leu
                     280                 285                 290

20   GAA GAT GAA GTA TAT GAA ACA GTT GTA GAT ACC TCT GAA GAA GAT AGT    1149
     Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu Glu Asp Ser
                 295                 300                 305

     TTT TCA TTA TGT TTT TCT AAA TGT AGA ACA AAA AAT CTA CAA AAA GTA    1197
25   Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu Gln Lys Val
         310                 315                 320

     AGA ACT AGC AAG ACT AGG AAA AAA ATT TTC CAT GAA GCA AAC GCT GAT    1245
     Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala Asn Ala Asp
30       325                 330                 335

     GAA TGT GAA AAA TCT AAA AAC CAA GTG AAA GAA AAA TAC TCA TTT GTA    1293
     Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr Ser Phe Val
     340                 345                 350                 355
35
     TCT GAA GTG GAA CCA AAT GAT ACT GAT CCA TTA GAT TCA AAT GTA GCA    1341
     Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser Asn Val Ala
                     360                 365                 370

40   CAT CAG AAG CCC TTT GAG AGT GGA AGT GAC AAA ATC TCC AAG GAA GTT    1389
     His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser Lys Glu Val
                 375                 380                 385

     GTA CCG TCT TTG GCC TGT GAA TGG TCT CAA CTA ACC CTT TCA GGT CTA    1437
45   Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu Ser Gly Leu
         390                 395                 400

     AAT GGA GCC CAG ATG GAG AAA ATA CCC CTA TTG CAT ATT TCT TCA TGT    1485
     Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile Ser Ser Cys
50       405                 410                 415

     GAC CAA AAT ATT TCA GAA AAA GAC CTA TTA GAC ACA GAG AAC AAA AGA    1533
     Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu Asn Lys Arg
     420                 425                 430                 435
55
     AAG AAA GAT TTT CTT ACT TCA GAG AAT TCT TTG CCA CGT ATT TCT AGC    1581
     Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg Ile Ser Ser
                     440                 445                 450

60   CTA CCA AAA TCG GAG AAG CCA TTA AAT GAG GAA ACA GTG GTA AAT AAG    1629
     Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val Val Asn Lys
                 455                 460                 465
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AGA GAT GAA GAG CAG CAT CTT GAA TCT CAT ACA GAC TGC ATT CTT GCA    1677
Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys Ile Leu Ala
          470                 475                 480

GTA AAG CAG GCA ATA TCT GGA ACT TCT CCA GTG GCT TCT TCA TTT CAG    1725
Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser Ser Phe Gln
     485                 490                 495

GGT ATC AAA AAG TCT ATA TTC AGA ATA AGA GAA TCA CCT AAA GAG ACT    1773
Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro Lys Glu Thr
500                 505                 510                 515

TTC AAT GCA AGT TTT TCA GGT CAT ATG ACT GAT CCA AAC TTT AAA AAA    1821
Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn Phe Lys Lys
                520                 525                 530

GAA ACT GAA GCC TCT GAA AGT GGA CTG GAA ATA CAT ACT GTT TGC TCA    1869
Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr Val Cys Ser
            535                 540                 545

CAG AAG GAG GAC TCC TTA TGT CCA AAT TTA ATT GAT AAT GGA AGC TGG    1917
Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn Gly Ser Trp
          550                 555                 560

CCA GCC ACC ACC ACA CAG AAT TCT GTA GCT TTG AAG AAT GCA GGT TTA    1965
Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn Ala Gly Leu
     565                 570                 575

ATA TCC ACT TTG AAA AAG AAA ACA AAT AAG TTT ATT TAT GCT ATA CAT    2013
Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr Ala Ile His
580                 585                 590                 595

GAT GAA ACA TCT TAT AAA GGA AAA AAA ATA CCG AAA GAC CAA AAA TCA    2061
Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp Gln Lys Ser
                600                 605                 610

GAA CTA ATT AAC TGT TCA GCC CAG TTT GAA GCA AAT GCT TTT GAA GCA    2109
Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala Phe Glu Ala
            615                 620                 625

CCA CTT ACA TTT GCA AAT GCT GAT TCA GGT TTA TTG CAT TCT TCT GTG    2157
Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His Ser Ser Val
          630                 635                 640

AAA AGA AGC TGT TCA CAG AAT GAT TCT GAA GAA CCA ACT TTG TCC TTA    2205
Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr Leu Ser Leu
     645                 650                 655

ACT AGC TCT TTT GGG ACA ATT CTG AGG AAA TGT TCT AGA AAT GAA ACA    2253
Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg Asn Glu Thr
660                 665                 670                 675

TGT TCT AAT AAT ACA GTA ATC TCT CAG GAT CTT GAT TAT AAA GAA GCA    2301
Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr Lys Glu Ala
                680                 685                 690

AAA TGT AAT AAG GAA AAA CTA CAG TTA TTT ATT ACC CCA GAA GCT GAT    2349
Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro Glu Ala Asp
            695                 700                 705
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TCT CTG TCA TGC CTG CAG GAA GGA CAG TGT GAA AAT GAT CCA AAA AGC    2397
Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp Pro Lys Ser
        710                 715                 720

AAA AAA GTT TCA GAT ATA AAA GAA GAG GTC TTG GCT GCA GCA TGT CAC    2445
Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala Ala Cys His
    725                 730                 735

CCA GTA CAA CAC TCA AAA GTG GAA TAC AGT GAT ACT GAC TTT CAA TCC    2493
Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp Phe Gln Ser
740                 745                 750                 755

CAG AAA AGT CTT TTA TAT GAT CAT GAA AAT GCC AGC ACT CTT ATT TTA    2541
Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr Leu Ile Leu
                760                 765                 770

ACT CCT ACT TCC AAG GAT GTT CTG TCA AAC CTA GTC ATG ATT TCT AGA    2589
Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met Ile Ser Arg
            775                 780                 785

GGC AAA GAA TCA TAC AAA ATG TCA GAC AAG CTC AAA GGT AAC AAT TAT    2637
Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly Asn Asn Tyr
        790                 795                 800

GAA TCT GAT GTT GAA TTA ACC AAA AAT ATT CCC ATG GAA AAG AAT CAA    2685
Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu Lys Asn Gln
    805                 810                 815

GAT GTA TGT GCT TTA AAT GAA AAT TAT AAA AAC GTT GAG CTG TTG CCA    2733
Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu Leu Leu Pro
820                 825                 830                 835

CCT GAA AAA TAC ATG AGA GTA GCA TCA CCT TCA AGA AAG GTA CAA TTC    2781
Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys Val Gln Phe
                840                 845                 850

AAC CAA AAC ACA AAT CTA AGA GTA ATC CAA AAA AAT CAA GAA GAA ACT    2829
Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln Glu Glu Thr
            855                 860                 865

ACT TCA ATT TCA AAA ATA ACT GTC AAT CCA GAC TCT GAA GAA CTT TTC    2877
Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu Glu Leu Phe
        870                 875                 880

TCA GAC AAT GAG AAT AAT TTT GTC TTC CAA ATA GCT AAT GAA AGG AAT    2925
Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Ile Ala Asn Glu Arg Asn
    885                 890                 895

AAT CTT GCT TTA GGA AAT ACT AAG GAA CTT CAT GAA ACA GAC TTG ACT    2973
Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr Asp Leu Thr
900                 905                 910                 915

TGT GTA AAC GAA CCC ATT TTC AAG AAC TCT ACC ATG GTT TTA TAT GGA    3021
Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val Leu Tyr Gly
                920                 925                 930

GAC ACA GGT GAT AAA CAA GCA ACC CAA GTG TCA ATT AAA AAA GAT TTG    3069
Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys Lys Asp Leu
            935                 940                 945

GTT TAT GTT CTT GCA GAG GAG AAC AAA AAT AGT GTA AAG CAG CAT ATA    3117
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Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys Gln His Ile
        950                 955                 960

AAA ATG ACT CTA GGT CAA GAT TTA AAA TCG GAC ATC TCC TTG AAT ATA    3165
Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser Leu Asn Ile
    965                 970                 975

GAT AAA ATA CCA GAA AAA AAT AAT GAT TAC ATG GAC AAA TGG GCA GGA    3213
Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asp Lys Trp Ala Gly
980                 985                 990                 995

CTC TTA GGT CCA ATT TCA AAT CAC AGT TTT GGA GGT AGC TTC AGA ACA    3261
Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser Phe Arg Thr
                1000                1005                1010

GCT TCA AAT AAG GAA ATC AAG CTC TCT GAA CAT AAC ATT AAG AAG AGC    3309
Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile Lys Lys Ser
            1015                1020                1025

AAA ATG TTC TTC AAA GAT ATT GAA GAA CAA TAT CCT ACT AGT TTA GCT    3357
Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr Ser Leu Ala
        1030                1035                1040

TGT GTT GAA ATT GTA AAT ACC TTG GCA TTA GAT AAT CAA AAG AAA CTG    3405
Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln Lys Lys Leu
    1045                1050                1055

AGC AAG CCT CAG TCA ATT AAT ACT GTA TCT GCA CAT TTA CAG AGT AGT    3453
Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu Gln Ser Ser
1060                1065                1070                1075

GTA GTT GTT TCT GAT TGT AAA AAT AGT CAT ATA ACC CCT CAG ATG TTA    3501
Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro Gln Met Leu
                1080                1085                1090

TTT TCC AAG CAG GAT TTT AAT TCA AAC CAT AAT TTA ACA CCT AGC CAA    3549
Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr Pro Ser Gln
            1095                1100                1105

AAG GCA GAA ATT ACA GAA CTT TCT ACT ATA TTA GAA GAA TCA GGA AGT    3597
Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu Ser Gly Ser
        1110                1115                1120

CAG TTT GAA TTT ACT CAG TTT AGA AAA CCA AGC TAC ATA TTG CAG AAG    3645
Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile Leu Gln Lys
    1125                1130                1135

AGT ACA TTT GAA GTG CCT GAA AAC CAG ATG ACT ATC TTA AAG ACC ACT    3693
Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu Lys Thr Thr
1140                1145                1150                1155

TCT GAG GAA TGC AGA GAT GCT GAT CTT CAT GTC ATA ATG AAT GCC CCA    3741
Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met Asn Ala Pro
                1160                1165                1170

TCG ATT GGT CAG GTA GAC AGC AGC AAG CAA TTT GAA GGT ACA GTT GAA    3789
Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly Thr Val Glu
            1175                1180                1185

ATT AAA CGG AAG TTT GCT GGC CTG TTG AAA AAT GAC TGT AAC AAA AGT    3837
Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys Asn Lys Ser
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          1190                1195                1200

     GCT TCT GGT TAT TTA ACA GAT GAA AAT GAA GTG GGG TTT AGG GGC TTT    3885
5    Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe Arg Gly Phe
        1205                1210                1215

     TAT TCT GCT CAT GGC ACA AAA CTG AAT GTT TCT ACT GAA GCT CTG CAA    3933
     Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu Ala Leu Gln
10  1220                1225                1230                1235

     AAA GCT GTG AAA CTG TTT AGT GAT ATT GAG AAT ATT AGT GAG GAA ACT    3981
     Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser Glu Glu Thr
                    1240                1245                1250
15
     TCT GCA GAG GTA CAT CCA ATA AGT TTA TCT TCA AGT AAA TGT CAT GAT    4029
     Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys Cys His Asp
              1255                1260                1265

20   TCT GTT GTT TCA ATG TTT AAG ATA GAA AAT CAT AAT GAT AAA ACT GTA    4077
     Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp Lys Thr Val
           1270                1275                1280

     AGT GAA AAA AAT AAT AAA TGC CAA CTG ATA TTA CAA AAT AAT ATT GAA    4125
25   Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn Asn Ile Glu
        1285                1290                1295

     ATG ACT ACT GGC ACT TTT GTT GAA GAA ATT ACT GAA AAT TAC AAG AGA    4173
     Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn Tyr Lys Arg
30  1300                1305                1310                1315

     AAT ACT GAA AAT GAA GAT AAC AAA TAT ACT GCT GCC AGT AGA AAT TCT    4221
     Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser Arg Asn Ser
                    1320                1325                1330
35
     CAT AAC TTA GAA TTT GAT GGC AGT GAT TCA AGT AAA AAT GAT ACT GTT    4269
     His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn Asp Thr Val
              1335                1340                1345

40   TGT ATT CAT AAA GAT GAA ACG GAC TTG CTA TTT ACT GAT CAG CAC AAC    4317
     Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp Gln His Asn
           1350                1355                1360

     ATA TGT CTT AAA TTA TCT GGC CAG TTT ATG AAG GAG GGA AAC ACT CAG    4365
45   Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly Asn Thr Gln
        1365                1370                1375

     ATT AAA GAA GAT TTG TCA GAT TTA ACT TTT TTG GAA GTT GCG AAA GCT    4413
     Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val Ala Lys Ala
50  1380                1385                1390                1395

     CAA GAA GCA TGT CAT GGT AAT ACT TCA AAT AAA GAA CAG TTA ACT GCT    4461
     Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln Leu Thr Ala
                    1400                1405                1410
55
     ACT AAA ACG GAG CAA AAT ATA AAA GAT TTT GAG ACT TCT GAT ACA TTT    4509
     Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser Asp Thr Phe
              1415                1420                1425

60   TTT CAG ACT GCA AGT GGG AAA AAT ATT AGT GTC GCC AAA GAG TCA TTT    4557
     Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys Glu Ser Phe
           1430                1435                1440
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AAT AAA ATT GTA AAT TTC TTT GAT CAG AAA CCA GAA GAA TTG CAT AAC    4605
Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu Leu His Asn
    1445                1450                1455

TTT TCC TTA AAT TCT GAA TTA CAT TCT GAC ATA AGA AAG AAC AAA ATG    4653
Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys Asn Lys Met
1460                1465                1470                1475

GAC ATT CTA AGT TAT GAG GAA ACA GAC ATA GTT AAA CAC AAA ATA CTG    4701
Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His Lys Ile Leu
                1480                1485                1490

AAA GAA AGT GTC CCA GTT GGT ACT GGA AAT CAA CTA GTG ACC TTC CAG    4749
Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val Thr Phe Gln
            1495                1500                1505

GGA CAA CCC GAA CGT GAT GAA AAG ATC AAA GAA CCT ACT CTG TTG GGT    4797
Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr Leu Leu Gly
        1510                1515                1520

TTT CAT ACA GCT AGC GGG AAA AAA GTT AAA ATT GCA AAG GAA TCT TTG    4845
Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys Glu Ser Leu
    1525                1530                1535

GAC AAA GTG AAA AAC CTT TTT GAT GAA AAA GAG CAA GGT ACT AGT GAA    4893
Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly Thr Ser Glu
1540                1545                1550                1555

ATC ACC AGT TTT AGC CAT CAA TGG GCA AAG ACC CTA AAG TAC AGA GAG    4941
Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys Tyr Arg Glu
                1560                1565                1570

GCC TGT AAA GAC CTT GAA TTA GCA TGT GAG ACC ATT GAG ATC ACA GCT    4989
Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu Ile Thr Ala
            1575                1580                1585

GCC CCA AAG TGT AAA GAA ATG CAG AAT TCT CTC AAT AAT GAT AAA AAC    5037
Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn Asp Lys Asn
        1590                1595                1600

CTT GTT TCT ATT GAG ACT GTG GTG CCA CCT AAG CTC TTA AGT GAT AAT    5085
Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu Ser Asp Asn
    1605                1610                1615

TTA TGT AGA CAA ACT GAA AAT CTC AAA ACA TCA AAA AGT ATC TTT TTG    5133
Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser Ile Phe Leu
1620                1625                1630                1635

AAA GTT AAA GTA CAT GAA AAT GTA GAA AAA GAA ACA GCA AAA AGT CCT    5181
Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala Lys Ser Pro
                1640                1645                1650

GCA ACT TGT TAC ACA AAT CAG TCC CCT TAT TCA GTC ATT GAA AAT TCA    5229
Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile Glu Asn Ser
            1655                1660                1665

GCC TTA GCT TTT TAC ACA AGT TGT AGT AGA AAA ACT TCT GTG AGT CAG    5277
Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser Val Ser Gln
        1670                1675                1680
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ACT TCA TTA CTT GAA GCA AAA AAA TGG CTT AGA GAA GGA ATA TTT GAT    5325
Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly Ile Phe Asp
   1685                1690                1695

GGT CAA CCA GAA AGA ATA AAT ACT GCA GAT TAT GTA GGA AAT TAT TTG    5373
Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly Asn Tyr Leu
1700                1705                1710                1715

TAT GAA AAT AAT TCA AAC AGT ACT ATA GCT GAA AAT GAC AAA AAT CAT    5421
Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp Lys Asn His
                1720                1725                1730

CTC TCC GAA AAA CAA GAT ACT TAT TTA AGT AAC AGT AGC ATG TCT AAC    5469
Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser Met Ser Asn
            1735                1740                1745

AGC TAT TCC TAC CAT TCT GAT GAG GTA TAT AAT GAT TCA GGA TAT CTC    5517
Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser Gly Tyr Leu
        1750                1755                1760

TCA AAA AAT AAA CTT GAT TCT GGT ATT GAG CCA GTA TTG AAG AAT GTT    5565
Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu Lys Asn Val
   1765                1770                1775

GAA GAT CAA AAA AAC ACT AGT TTT TCC AAA GTA ATA TCC AAT GTA AAA    5613
Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser Asn Val Lys
1780                1785                1790                1795

GAT GCA AAT GCA TAC CCA CAA ACT GTA AAT GAA GAT ATT TGC GTT GAG    5661
Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile Cys Val Glu
                1800                1805                1810

GAA CTT GTG ACT AGC TCT TCA CCC TGC AAA AAT AAA AAT GCA GCC ATT    5709
Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn Ala Ala Ile
            1815                1820                1825

AAA TTG TCC ATA TCT AAT AGT AAT AAT TTT GAG GTA GGG CCA CCT GCA    5757
Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly Pro Pro Ala
        1830                1835                1840

TTT AGG ATA GCC AGT GGT AAA ATC GTT TGT GTT TCA CAT GAA ACA ATT    5805
Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His Glu Thr Ile
   1845                1850                1855

AAA AAA GTG AAA GAC ATA TTT ACA GAC AGT TTC AGT AAA GTA ATT AAG    5853
Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys Val Ile Lys
1860                1865                1870                1875

GAA AAC AAC GAG AAT AAA TCA AAA ATT TGC CAA ACG AAA ATT ATG GCA    5901
Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys Ile Met Ala
                1880                1885                1890

GGT TGT TAC GAG GCA TTG GAT GAT TCA GAG GAT ATT CTT CAT AAC TCT    5949
Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu His Asn Ser
            1895                1900                1905

CTA GAT AAT GAT GAA TGT AGC ACG CAT TCA CAT AAG GTT TTT GCT GAC    5997
Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val Phe Ala Asp
        1910                1915                1920

ATT CAG AGT GAA GAA ATT TTA CAA CAT AAC CAA AAT ATG TCT GGA TTG    6045
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Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met Ser Gly Leu
   1925                1930                1935

GAG AAA GTT TCT AAA ATA TCA CCT TGT GAT GTT AGT TTG GAA ACT TCA    6093
Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu Glu Thr Ser
1940                1945                1950                1955

GAT ATA TGT AAA TGT AGT ATA GGG AAG CTT CAT AAG TCA GTC TCA TCT    6141
Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser Val Ser Ser
                1960                1965                1970

GCA AAT ACT TGT GGG ATT TTT AGC ACA GCA AGT GGA AAA TCT GTC CAG    6189
Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys Ser Val Gln
            1975                1980                1985

GTA TCA GAT GCT TCA TTA CAA AAC GCA AGA CAA GTG TTT TCT GAA ATA    6237
Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe Ser Glu Ile
        1990                1995                2000

GAA GAT AGT ACC AAG CAA GTC TTT TCC AAA GTA TTG TTT AAA AGT AAC    6285
Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe Lys Ser Asn
    2005                2010                2015

GAA CAT TCA GAC CAG CTC ACA AGA GAA GAA AAT ACT GCT ATA CGT ACT    6333
Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala Ile Arg Thr
2020                2025                2030                2035

CCA GAA CAT TTA ATA TCC CAA AAA GGC TTT TCA TAT AAT GTG GTA AAT    6381
Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn Val Val Asn
                2040                2045                2050

TCA TCT GCT TTC TCT GGA TTT AGT ACA GCA AGT GGA AAG CAA GTT TCC    6429
Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys Gln Val Ser
            2055                2060                2065

ATT TTA GAA AGT TCC TTA CAC AAA GTT AAG GGA GTG TTA GAG GAA TTT    6477
Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu Glu Glu Phe
        2070                2075                2080

GAT TTA ATC AGA ACT GAG CAT AGT CTT CAC TAT TCA CCT ACG TCT AGA    6525
Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro Thr Ser Arg
    2085                2090                2095

CAA AAT GTA TCA AAA ATA CTT CCT CGT GTT GAT AAG AGA AAC CCA GAG    6573
Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg Asn Pro Glu
2100                2105                2110                2115

CAC TGT GTA AAC TCA GAA ATG GAA AAA ACC TGC AGT AAA GAA TTT AAA    6621
His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys Glu Phe Lys
                2120                2125                2130

TTA TCA AAT AAC TTA AAT GTT GAA GGT GGT TCT TCA GAA AAT AAT CAC    6669
Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu Asn Asn His
            2135                2140                2145

TCT ATT AAA GTT TCT CCA TAT CTC TCT CAA TTT CAA CAA GAC AAA CAA    6717
Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln Asp Lys Gln
        2150                2155                2160

CAG TTG GTA TTA GGA ACC AAA GTC TCA CTT GTT GAG AAC ATT CAT GTT    6765
Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn Ile His Val
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      2165                2170                2175

   TTG GGA AAA GAA CAG GCT TCA CCT AAA AAC GTA AAA ATG GAA ATT GGT    6813
5  Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met Glu Ile Gly
  2180                2185                2190                2195

   AAA ACT GAA ACT TTT TCT GAT GTT CCT GTG AAA ACA AAT ATA GAA GTT    6861
   Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn Ile Glu Val
10                2200                2205                2210

   TGT TCT ACT TAC TCC AAA GAT TCA GAA AAC TAC TTT GAA ACA GAA GCA    6909
   Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu Thr Glu Ala
             2215                2220                2225
15
   GTA GAA ATT GCT AAA GCT TTT ATG GAA GAT GAT GAA CTG ACA GAT TCT    6957
   Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu Thr Asp Ser
        2230                2235                2240

20 AAA CTG CCA AGT CAT GCC ACA CAT TCT CTT TTT ACA TGT CCC GAA AAT    7005
   Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys Pro Glu Asn
     2245                2250                2255

   GAG GAA ATG GTT TTG TCA AAT TCA AGA ATT GGA AAA AGA AGA GGA GAG    7053
25 Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg Arg Gly Glu
  2260                2265                2270                2275

   CCC CTT ATC TTA GTG GGA GAA CCC TCA ATC AAA AGA AAC TTA TTA AAT    7101
   Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn Leu Leu Asn
30                2280                2285                2290

   GAA TTT GAC AGG ATA ATA GAA AAT CAA GAA AAA TCC TTA AAG GCT TCA    7149
   Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu Lys Ala Ser
             2295                2300                2305
35
   AAA AGC ACT CCA GAT GGC ACA ATA AAA GAT CGA AGA TTG TTT ATG CAT    7197
   Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu Phe Met His
        2310                2315                2320

40 CAT GTT TCT TTA GAG CCG ATT ACC TGT GTA CCC TTT CGC ACA ACT AAG    7245
   His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg Thr Thr Lys
     2325                2330                2335

   GAA CGT CAA GAG ATA CAG AAT CCA AAT TTT ACC GCA CCT GGT CAA GAA    7293
45 Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro Gly Gln Glu
  2340                2345                2350                2355

   TTT CTG TCT AAA TCT CAT TTG TAT GAA CAT CTG ACT TTG GAA AAA TCT    7341
   Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu Glu Lys Ser
50                2360                2365                2370

   TCA AGC AAT TTA GCA GTT TCA GGA CAT CCA TTT TAT CAA GTT TCT GCT    7389
   Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln Val Ser Ala
             2375                2380                2385
55
   ACA AGA AAT GAA AAA ATG AGA CAC TTG ATT ACT ACA GGC AGA CCA ACC    7437
   Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly Arg Pro Thr
        2390                2395                2400

60 AAA GTC TTT GTT CCA CCT TTT AAA ACT AAA TCA CAT TTT CAC AGA GTT    7485
   Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe His Arg Val
     2405                2410                2415
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GAA CAG TGT GTT AGG AAT ATT AAC TTG GAG GAA AAC AGA CAA AAG CAA    7533
Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg Gln Lys Gln
2420                2425                2430                2435

AAC ATT GAT GGA CAT GGC TCT GAT GAT AGT AAA AAT AAG ATT AAT GAC    7581
Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys Ile Asn Asp
                2440                2445                2450

AAT GAG ATT CAT CAG TTT AAC AAA AAC AAC TCC AAT CAA GCA GCA GCT    7629
Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln Ala Ala Ala
            2455                2460                2465

GTA ACT TTC ACA AAG TGT GAA GAA GAA CCT TTA GAT TTA ATT ACA AGT    7677
Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu Ile Thr Ser
        2470                2475                2480

CTT CAG AAT GCC AGA GAT ATA CAG GAT ATG CGA ATT AAG AAG AAA CAA    7725
Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys Lys Lys Gln
    2485                2490                2495

AGG CAA CGC GTC TTT CCA CAG CCA GGC AGT CTG TAT CTT GCA AAA ACA    7773
Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu Ala Lys Thr
2500                2505                2510                2515

TCC ACT CTG CCT CGA ATC TCT CTG AAA GCA GCA GTA GGA GGC CAA GTT    7821
Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly Gly Gln Val
                2520                2525                2530

CCC TCT GCG TGT TCT CAT AAA CAG CTG TAT ACG TAT GGC GTT TCT AAA    7869
Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly Val Ser Lys
            2535                2540                2545

CAT TGC ATA AAA ATT AAC AGC AAA AAT GCA GAG TCT TTT CAG TTT CAC    7917
His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe Gln Phe His
        2550                2555                2560

ACT GAA GAT TAT TTT GGT AAG GAA AGT TTA TGG ACT GGA AAA GGA ATA    7965
Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly Lys Gly Ile
    2565                2570                2575

CAG TTG GCT GAT GGT GGA TGG CTC ATA CCC TCC AAT GAT GGA AAG GCT    8013
Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp Gly Lys Ala
2580                2585                2590                2595

GGA AAA GAA GAA TTT TAT AGG GCT CTG TGT GAC ACT CCA GGT GTG GAT    8061
Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro Gly Val Asp
                2600                2605                2610

CCA AAG CTT ATT TCT AGA ATT TGG GTT TAT AAT CAC TAT AGA TGG ATC    8109
Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr Arg Trp Ile
            2615                2620                2625

ATA TGG AAA CTG GCA GCT ATG GAA TGT GCC TTT CCT AAG GAA TTT GCT    8157
Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys Glu Phe Ala
        2630                2635                2640

AAT AGA TGC CTA AGC CCA GAA AGG GTG CTT CTT CAA CTA AAA TAC AGA    8205
Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu Lys Tyr Arg
    2645                2650                2655
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TAT GAT ACG GAA ATT GAT AGA AGC AGA AGA TCG GCT ATA AAA AAG ATA    8253
Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile Lys Lys Ile
2660                2665                2670                2675

ATG GAA AGG GAT GAC ACA GCT GCA AAA ACA CTT GTT CTC TGT GTT TCT    8301
Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu Cys Val Ser
                2680                2685                2690

GAC ATA ATT TCA TTG AGC GCA AAT ATA TCT GAA ACT TCT AGC AAT AAA    8349
Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser Ser Asn Lys
            2695                2700                2705

ACT AGT AGT GCA GAT ACC CAA AAA GTG GCC ATT ATT GAA CTT ACA GAT    8397
Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu Leu Thr Asp
        2710                2715                2720

GGG TGG TAT GCT GTT AAG GCC CAG TTA GAT CCT CCC CTC TTA GCT GTC    8445
Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu Leu Ala Val
    2725                2730                2735

TTA AAG AAT GGC AGA CTG ACA GTT GGT CAG AAG ATT ATT CTT CAT GGA    8493
Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile Leu His Gly
2740                2745                2750                2755

GCA GAA CTG GTG GGC TCT CCT GAT GCC TGT ACA CCT CTT GAA GCC CCA    8541
Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu Glu Ala Pro
                2760                2765                2770

GAA TCT CTT ATG TTA AAG ATT TCT GCT AAC AGT ACT CGG CCT GCT CGC    8589
Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg Pro Ala Arg
            2775                2780                2785

TGG TAT ACC AAA CTT GGA TTC TTT CCT GAC CCT AGA CCT TTT CCT CTG    8637
Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro Phe Pro Leu
        2790                2795                2800

CCC TTA TCA TCG CTT TTC AGT GAT GGA GGA AAT GTT GGT TGT GTT GAT    8685
Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly Cys Val Asp
    2805                2810                2815

GTA ATT ATT CAA AGA GCA TAC CCT ATA CAG TGG ATG GAG AAG ACA TCA    8733
Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu Lys Thr Ser
2820                2825                2830                2835

TCT GGA TTA TAC ATA TTT CGC AAT GAA AGA GAG GAA GAA AAG GAA GCA    8781
Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu Lys Glu Ala
                2840                2845                2850

GCA AAA TAT GTG GAG GCC CAA CAA AAG AGA CTA GAA GCC TTA TTC ACT    8829
Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala Leu Phe Thr
            2855                2860                2865

AAA ATT CAG GAG GAA TTT GAA GAA CAT GAA GAA AAC ACA ACA AAA CCA    8877
Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr Thr Lys Pro
        2870                2875                2880

TAT TTA CCA TCA CGT GCA CTA ACA AGA CAG CAA GTT CGT GCT TTG CAA    8925
Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg Ala Leu Gln
    2885                2890                2895

GAT GGT GCA GAG CTT TAT GAA GCA GTG AAG AAT GCA GCA GAC CCA GCT    8973
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     Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala Asp Pro Ala
    2900                2905                2910                2915

 5  TAC CTT GAG GGT TAT TTC AGT GAA GAG CAG TTA AGA GCC TTG AAT AAT    9021
    Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala Leu Asn Asn
                   2920                2925                2930

    CAC AGG CAA ATG TTG AAT GAT AAG AAA CAA GCT CAG ATC CAG TTG GAA    9069
10  His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile Gln Leu Glu
              2935                2940                2945

    ATT AGG AAG ACC ATG GAA TCT GCT GAA CAA AAG GAA CAA GGT TTA TCA    9117
    Ile Arg Lys Thr Met Glu Ser Ala Glu Gln Lys Glu Gln Gly Leu Ser
15        2950                2955                2960

    AGG GAT GTC ACA ACC GTG TGG AAG TTG CGT ATT GTA AGC TAT TCA AAA    9165
    Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser Tyr Ser Lys
       2965                2970                2975
20
    AAA GAA AAA GAT TCA GTT ATA CTG AGT ATT TGG CGT CCA TCA TCA GAT    9213
    Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro Ser Ser Asp
    2980                2985                2990                2995

25  TTA TAT TCT CTG TTA ACA GAA GGA AAG AGA TAC AGA ATT TAT CAT CTT    9261
    Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile Tyr His Leu
                   3000                3005                3010

    GCA ACT TCA AAA TCT AAA AGT AAA TCT GAA AGA GCT AAC ATA CAG TTA    9309
30  Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn Ile Gln Leu
              3015                3020                3025

    GCA GCG ACA AAA AAA ACT CAG TAT CAA CAA CTA CCG GTT TCA GAT GAA    9357
    Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val Ser Asp Glu
35        3030                3035                3040

    ATT TTA TTT CAG ATT TAC CAG CCA CGG GAG CCC CTT CAC TTC AGC AAA    9405
    Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His Phe Ser Lys
       3045                3050                3055
40
    TTT TTA GAT CCA GAC TTT CAG CCA TCT TGT TCT GAG GTG GAC CTA ATA    9453
    Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val Asp Leu Ile
    3060                3065                3070                3075

45  GGA TTT GTC GTT TCT GTT GTG AAA AAA ACA GGA CTT GCC CCT TTC GTC    9501
    Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala Pro Phe Val
                   3080                3085                3090

    TAT TTG TCA GAC GAA TGT TAC AAT TTA CTG GCA ATA AAG TTT TGG ATA    9549
50  Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys Phe Trp Ile
              3095                3100                3105

    GAC CTT AAT GAG GAC ATT ATT AAG CCT CAT ATG TTA ATT GCT GCA AGC    9597
    Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile Ala Ala Ser
55        3110                3115                3120

    AAC CTC CAG TGG CGA CCA GAA TCC AAA TCA GGC CTT CTT ACT TTA TTT    9645
    Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu Thr Leu Phe
       3125                3130                3135
60
    GCT GGA GAT TTT TCT GTG TTT TCT GCT AGT CCA AAA GAG GGC CAC TTT    9693
    Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu Gly His Phe
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3140                3145                3150                3155

CAA GAG ACA TTC AAC AAA ATG AAA AAT ACT GTT GAG AAT ATT GAC ATA    9741
Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn Ile Asp Ile
                3160                3165                3170

CTT TGC AAT GAA GCA GAA AAC AAG CTT ATG CAT ATA CTG CAT GCA AAT    9789
Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu His Ala Asn
            3175                3180                3185

GAT CCC AAG TGG TCC ACC CCA ACT AAA GAC TGT ACT TCA GGG CCG TAC    9837
Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser Gly Pro Tyr
        3190                3195                3200

ACT GCT CAA ATC ATT CCT GGT ACA GGA AAC AAG CTT CTG ATG TCT TCT    9885
Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu Met Ser Ser
    3205                3210                3215

CCT AAT TGT GAG ATA TAT TAT CAA AGT CCT TTA TCA CTT TGT ATG GCC    9933
Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu Cys Met Ala
3220                3225                3230                3235

AAA AGG AAG TCT GTT TCC ACA CCT GTC TCA GCC CAG ATG ACT TCA AAG    9981
Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met Thr Ser Lys
                3240                3245                3250

TCT TGT AAA GGG GAG AAA GAG ATT GAT GAC CAA AAG AAC TGC AAA AAG   10029
Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn Cys Lys Lys
            3255                3260                3265

AGA AGA GCC TTG GAT TTC TTG AGT AGA CTG CCT TTA CCT CCA CCT GTT   10077
Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro Pro Pro Val
        3270                3275                3280

AGT CCC ATT TGT ACA TTT GTT TCT CCG GCT GCA CAG AAG GCA TTT CAG   10125
Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys Ala Phe Gln
    3285                3290                3295

CCA CCA AGG AGT TGT GGC ACC AAA TAC GAA ACA CCC ATA AAG AAA AAA   10173
Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile Lys Lys Lys
3300                3305                3310                3315

GAA CTG AAT TCT CCT CAG ATG ACT CCA TTT AAA AAA TTC AAT GAA ATT   10221
Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe Asn Glu Ile
                3320                3325                3330

TCT CTT TTG GAA AGT AAT TCA ATA GCT GAC GAA GAA CTT GCA TTG ATA   10269
Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile
            3335                3340                3345

AAT ACC CAA GCT CTT TTG TCT GGT TCA ACA GGA GAA AAA CAA TTT ATA   10317
Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys Gln Phe Ile
        3350                3355                3360

TCT GTC AGT GAA TCC ACT AGG ACT GCT CCC ACC AGT TCA GAA GAT TAT   10365
Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp Tyr
    3365                3370                3375

CTC AGA CTG AAA CGA CGT TGT ACT ACA TCT CTG ATC AAA GAA CAG GAG   10413
Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu Gln Glu
3380                3385                3390                3395
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AGT TCC CAG GCC AGT ACG GAA GAA TGT GAG AAA AAT AAG CAG GAC ACA   10461
Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys Gln Asp Thr
                3400                3405                3410

ATT ACA ACT AAA AAA TAT ATC TAA                                  10485
Ile Thr Thr Lys Lys Tyr Ile
          3415
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(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3418 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

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Met Pro Ile Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys
 1               5                  10                  15
Thr Arg Cys Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe
            20                  25                  30
Glu Glu Leu Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu
        35                  40                  45
Glu Ser Glu His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr
    50                  55                  60
Pro Gln Arg Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile
65                  70                  75                  80
Phe Lys Glu Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys
                85                  90                  95
Glu Leu Asp Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser
            100                 105                 110
Arg His Lys Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp
        115                 120                 125
Asp Val Ser Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val
    130                 135                 140
Val Leu Gln Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val
145                 150                 155                 160
Cys Gly Ser Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr
                165                 170                 175
Pro Lys His Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met
            180                 185                 190
Ser Trp Ser Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val
        195                 200                 205
Leu Ile Val Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp
    210                 215                 220
Thr Thr Ala Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu
225                 230                 235                 240
Lys Lys Asn Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr
                245                 250                 255
Asn Gln Arg Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn
            260                 265                 270
Ser Phe Lys Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro
        275                 280                 285
His Val Leu Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu
    290                 295                 300
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Glu Asp Ser Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu
305 310 315 320
Gln Lys Val Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala
325 330 335
Asn Ala Asp Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr
340 345 350
Ser Phe Val Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser
355 360 365
Asn Val Ala His Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser
370 375 380
Lys Glu Val Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu
385 390 395 400
Ser Gly Leu Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile
405 410 415
Ser Ser Cys Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu
420 425 430
Asn Lys Arg Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg
435 440 445
Ile Ser Ser Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val
450 455 460
Val Asn Lys Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys
465 470 475 480
Ile Leu Ala Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser
485 490 495
Ser Phe Gln Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro
500 505 510
Lys Glu Thr Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn
515 520 525
Phe Lys Lys Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr
530 535 540
Val Cys Ser Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn
545 550 555 560
Gly Ser Trp Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn
565 570 575
Ala Gly Leu Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr
580 585 590
Ala Ile His Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp
595 600 605
Gln Lys Ser Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala
610 615 620
Phe Glu Ala Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His
625 630 635 640
Ser Ser Val Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr
645 650 655
Leu Ser Leu Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg
660 665 670
Asn Glu Thr Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr
675 680 685
Lys Glu Ala Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro
690 695 700
Glu Ala Asp Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp
705 710 715 720
Pro Lys Ser Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala
725 730 735
Ala Cys His Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp
740 745 750
Phe Gln Ser Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr
755 760 765
Leu Ile Leu Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met
770 775 780
Ile Ser Arg Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly

785 790 795 800
Asn Asn Tyr Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu
805 810 815
Lys Asn Gln Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu
820 825 830
Leu Leu Pro Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys
835 840 845
Val Gln Phe Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln
850 855 860
Glu Glu Thr Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu
865 870 875 880
Glu Leu Phe Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Ile Ala Asn
885 890 895
Glu Arg Asn Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr
900 905 910
Asp Leu Thr Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val
915 920 925
Leu Tyr Gly Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys
930 935 940
Lys Asp Leu Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys
945 950 955 960
Gln His Ile Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser
965 970 975
Leu Asn Ile Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asp Lys
980 985 990
Trp Ala Gly Leu Leu Gly Pro Ile Ser Asn His Ser Phe Gly Gly Ser
995 1000 1005
Phe Arg Thr Ala Ser Asn Lys Glu Ile Lys Leu Ser Glu His Asn Ile
1010 1015 1020
Lys Lys Ser Lys Met Phe Phe Lys Asp Ile Glu Glu Gln Tyr Pro Thr
1025 1030 1035 104
Ser Leu Ala Cys Val Glu Ile Val Asn Thr Leu Ala Leu Asp Asn Gln
1045 1050 1055
Lys Lys Leu Ser Lys Pro Gln Ser Ile Asn Thr Val Ser Ala His Leu
1060 1065 1070
Gln Ser Ser Val Val Val Ser Asp Cys Lys Asn Ser His Ile Thr Pro
1075 1080 1085
Gln Met Leu Phe Ser Lys Gln Asp Phe Asn Ser Asn His Asn Leu Thr
1090 1095 1100
Pro Ser Gln Lys Ala Glu Ile Thr Glu Leu Ser Thr Ile Leu Glu Glu
1105 1110 1115 112
Ser Gly Ser Gln Phe Glu Phe Thr Gln Phe Arg Lys Pro Ser Tyr Ile
1125 1130 1135
Leu Gln Lys Ser Thr Phe Glu Val Pro Glu Asn Gln Met Thr Ile Leu
1140 1145 1150
Lys Thr Thr Ser Glu Glu Cys Arg Asp Ala Asp Leu His Val Ile Met
1155 1160 1165
Asn Ala Pro Ser Ile Gly Gln Val Asp Ser Ser Lys Gln Phe Glu Gly
1170 1175 1180
Thr Val Glu Ile Lys Arg Lys Phe Ala Gly Leu Leu Lys Asn Asp Cys
1185 1190 1195 120
Asn Lys Ser Ala Ser Gly Tyr Leu Thr Asp Glu Asn Glu Val Gly Phe
1205 1210 1215
Arg Gly Phe Tyr Ser Ala His Gly Thr Lys Leu Asn Val Ser Thr Glu
1220 1225 1230
Ala Leu Gln Lys Ala Val Lys Leu Phe Ser Asp Ile Glu Asn Ile Ser
1235 1240 1245
Glu Glu Thr Ser Ala Glu Val His Pro Ile Ser Leu Ser Ser Ser Lys
1250 1255 1260
Cys His Asp Ser Val Val Ser Met Phe Lys Ile Glu Asn His Asn Asp
1265 1270 1275 128

Lys Thr Val Ser Glu Lys Asn Asn Lys Cys Gln Leu Ile Leu Gln Asn
1285 1290 1295
Asn Ile Glu Met Thr Thr Gly Thr Phe Val Glu Glu Ile Thr Glu Asn
1300 1305 1310
Tyr Lys Arg Asn Thr Glu Asn Glu Asp Asn Lys Tyr Thr Ala Ala Ser
1315 1320 1325
Arg Asn Ser His Asn Leu Glu Phe Asp Gly Ser Asp Ser Ser Lys Asn
1330 1335 1340
Asp Thr Val Cys Ile His Lys Asp Glu Thr Asp Leu Leu Phe Thr Asp
1345 1350 1355 136
Gln His Asn Ile Cys Leu Lys Leu Ser Gly Gln Phe Met Lys Glu Gly
1365 1370 1375
Asn Thr Gln Ile Lys Glu Asp Leu Ser Asp Leu Thr Phe Leu Glu Val
1380 1385 1390
Ala Lys Ala Gln Glu Ala Cys His Gly Asn Thr Ser Asn Lys Glu Gln
1395 1400 1405
Leu Thr Ala Thr Lys Thr Glu Gln Asn Ile Lys Asp Phe Glu Thr Ser
1410 1415 1420
Asp Thr Phe Phe Gln Thr Ala Ser Gly Lys Asn Ile Ser Val Ala Lys
1425 1430 1435 144
Glu Ser Phe Asn Lys Ile Val Asn Phe Phe Asp Gln Lys Pro Glu Glu
1445 1450 1455
Leu His Asn Phe Ser Leu Asn Ser Glu Leu His Ser Asp Ile Arg Lys
1460 1465 1470
Asn Lys Met Asp Ile Leu Ser Tyr Glu Glu Thr Asp Ile Val Lys His
1475 1480 1485
Lys Ile Leu Lys Glu Ser Val Pro Val Gly Thr Gly Asn Gln Leu Val
1490 1495 1500
Thr Phe Gln Gly Gln Pro Glu Arg Asp Glu Lys Ile Lys Glu Pro Thr
1505 1510 1515 152
Leu Leu Gly Phe His Thr Ala Ser Gly Lys Lys Val Lys Ile Ala Lys
1525 1530 1535
Glu Ser Leu Asp Lys Val Lys Asn Leu Phe Asp Glu Lys Glu Gln Gly
1540 1545 1550
Thr Ser Glu Ile Thr Ser Phe Ser His Gln Trp Ala Lys Thr Leu Lys
1555 1560 1565
Tyr Arg Glu Ala Cys Lys Asp Leu Glu Leu Ala Cys Glu Thr Ile Glu
1570 1575 1580
Ile Thr Ala Ala Pro Lys Cys Lys Glu Met Gln Asn Ser Leu Asn Asn
1585 1590 1595 160
Asp Lys Asn Leu Val Ser Ile Glu Thr Val Val Pro Pro Lys Leu Leu
1605 1610 1615
Ser Asp Asn Leu Cys Arg Gln Thr Glu Asn Leu Lys Thr Ser Lys Ser
1620 1625 1630
Ile Phe Leu Lys Val Lys Val His Glu Asn Val Glu Lys Glu Thr Ala
1635 1640 1645
Lys Ser Pro Ala Thr Cys Tyr Thr Asn Gln Ser Pro Tyr Ser Val Ile
1650 1655 1660
Glu Asn Ser Ala Leu Ala Phe Tyr Thr Ser Cys Ser Arg Lys Thr Ser
1665 1670 1675 168
Val Ser Gln Thr Ser Leu Leu Glu Ala Lys Lys Trp Leu Arg Glu Gly
1685 1690 1695
Ile Phe Asp Gly Gln Pro Glu Arg Ile Asn Thr Ala Asp Tyr Val Gly
1700 1705 1710
Asn Tyr Leu Tyr Glu Asn Asn Ser Asn Ser Thr Ile Ala Glu Asn Asp
1715 1720 1725
Lys Asn His Leu Ser Glu Lys Gln Asp Thr Tyr Leu Ser Asn Ser Ser
1730 1735 1740
Met Ser Asn Ser Tyr Ser Tyr His Ser Asp Glu Val Tyr Asn Asp Ser
1745 1750 1755 176
Gly Tyr Leu Ser Lys Asn Lys Leu Asp Ser Gly Ile Glu Pro Val Leu

1765 1770 1775
Lys Asn Val Glu Asp Gln Lys Asn Thr Ser Phe Ser Lys Val Ile Ser
1780 1785 1790
Asn Val Lys Asp Ala Asn Ala Tyr Pro Gln Thr Val Asn Glu Asp Ile
1795 1800 1805
Cys Val Glu Glu Leu Val Thr Ser Ser Ser Pro Cys Lys Asn Lys Asn
1810 1815 1820
Ala Ala Ile Lys Leu Ser Ile Ser Asn Ser Asn Asn Phe Glu Val Gly
1825 1830 1835 184
Pro Pro Ala Phe Arg Ile Ala Ser Gly Lys Ile Val Cys Val Ser His
1845 1850 1855
Glu Thr Ile Lys Lys Val Lys Asp Ile Phe Thr Asp Ser Phe Ser Lys
1860 1865 1870
Val Ile Lys Glu Asn Asn Glu Asn Lys Ser Lys Ile Cys Gln Thr Lys
1875 1880 1885
Ile Met Ala Gly Cys Tyr Glu Ala Leu Asp Asp Ser Glu Asp Ile Leu
1890 1895 1900
His Asn Ser Leu Asp Asn Asp Glu Cys Ser Thr His Ser His Lys Val
1905 1910 1915 192
Phe Ala Asp Ile Gln Ser Glu Glu Ile Leu Gln His Asn Gln Asn Met
1925 1930 1935
Ser Gly Leu Glu Lys Val Ser Lys Ile Ser Pro Cys Asp Val Ser Leu
1940 1945 1950
Glu Thr Ser Asp Ile Cys Lys Cys Ser Ile Gly Lys Leu His Lys Ser
1955 1960 1965
Val Ser Ser Ala Asn Thr Cys Gly Ile Phe Ser Thr Ala Ser Gly Lys
1970 1975 1980
Ser Val Gln Val Ser Asp Ala Ser Leu Gln Asn Ala Arg Gln Val Phe
1985 1990 1995 200
Ser Glu Ile Glu Asp Ser Thr Lys Gln Val Phe Ser Lys Val Leu Phe
2005 2010 2015
Lys Ser Asn Glu His Ser Asp Gln Leu Thr Arg Glu Glu Asn Thr Ala
2020 2025 2030
Ile Arg Thr Pro Glu His Leu Ile Ser Gln Lys Gly Phe Ser Tyr Asn
2035 2040 2045
Val Val Asn Ser Ser Ala Phe Ser Gly Phe Ser Thr Ala Ser Gly Lys
2050 2055 2060
Gln Val Ser Ile Leu Glu Ser Ser Leu His Lys Val Lys Gly Val Leu
2065 2070 2075 208
Glu Glu Phe Asp Leu Ile Arg Thr Glu His Ser Leu His Tyr Ser Pro
2085 2090 2095
Thr Ser Arg Gln Asn Val Ser Lys Ile Leu Pro Arg Val Asp Lys Arg
2100 2105 2110
Asn Pro Glu His Cys Val Asn Ser Glu Met Glu Lys Thr Cys Ser Lys
2115 2120 2125
Glu Phe Lys Leu Ser Asn Asn Leu Asn Val Glu Gly Gly Ser Ser Glu
2130 2135 2140
Asn Asn His Ser Ile Lys Val Ser Pro Tyr Leu Ser Gln Phe Gln Gln
2145 2150 2155 216
Asp Lys Gln Gln Leu Val Leu Gly Thr Lys Val Ser Leu Val Glu Asn
2165 2170 2175
Ile His Val Leu Gly Lys Glu Gln Ala Ser Pro Lys Asn Val Lys Met
2180 2185 2190
Glu Ile Gly Lys Thr Glu Thr Phe Ser Asp Val Pro Val Lys Thr Asn
2195 2200 2205
Ile Glu Val Cys Ser Thr Tyr Ser Lys Asp Ser Glu Asn Tyr Phe Glu
2210 2215 2220
Thr Glu Ala Val Glu Ile Ala Lys Ala Phe Met Glu Asp Asp Glu Leu
2225 2230 2235 224
Thr Asp Ser Lys Leu Pro Ser His Ala Thr His Ser Leu Phe Thr Cys
2245 2250 2255

Pro Glu Asn Glu Glu Met Val Leu Ser Asn Ser Arg Ile Gly Lys Arg
2260 2265 2270
Arg Gly Glu Pro Leu Ile Leu Val Gly Glu Pro Ser Ile Lys Arg Asn
2275 2280 2285
Leu Leu Asn Glu Phe Asp Arg Ile Ile Glu Asn Gln Glu Lys Ser Leu
2290 2295 2300
Lys Ala Ser Lys Ser Thr Pro Asp Gly Thr Ile Lys Asp Arg Arg Leu
2305 2310 2315 232
Phe Met His His Val Ser Leu Glu Pro Ile Thr Cys Val Pro Phe Arg
2325 2330 2335
Thr Thr Lys Glu Arg Gln Glu Ile Gln Asn Pro Asn Phe Thr Ala Pro
2340 2345 2350
Gly Gln Glu Phe Leu Ser Lys Ser His Leu Tyr Glu His Leu Thr Leu
2355 2360 2365
Glu Lys Ser Ser Ser Asn Leu Ala Val Ser Gly His Pro Phe Tyr Gln
2370 2375 2380
Val Ser Ala Thr Arg Asn Glu Lys Met Arg His Leu Ile Thr Thr Gly
2385 2390 2395 240
Arg Pro Thr Lys Val Phe Val Pro Pro Phe Lys Thr Lys Ser His Phe
2405 2410 2415
His Arg Val Glu Gln Cys Val Arg Asn Ile Asn Leu Glu Glu Asn Arg
2420 2425 2430
Gln Lys Gln Asn Ile Asp Gly His Gly Ser Asp Asp Ser Lys Asn Lys
2435 2440 2445
Ile Asn Asp Asn Glu Ile His Gln Phe Asn Lys Asn Asn Ser Asn Gln
2450 2455 2460
Ala Ala Ala Val Thr Phe Thr Lys Cys Glu Glu Glu Pro Leu Asp Leu
2465 2470 2475 248
Ile Thr Ser Leu Gln Asn Ala Arg Asp Ile Gln Asp Met Arg Ile Lys
2485 2490 2495
Lys Lys Gln Arg Gln Arg Val Phe Pro Gln Pro Gly Ser Leu Tyr Leu
2500 2505 2510
Ala Lys Thr Ser Thr Leu Pro Arg Ile Ser Leu Lys Ala Ala Val Gly
2515 2520 2525
Gly Gln Val Pro Ser Ala Cys Ser His Lys Gln Leu Tyr Thr Tyr Gly
2530 2535 2540
Val Ser Lys His Cys Ile Lys Ile Asn Ser Lys Asn Ala Glu Ser Phe
2545 2550 2555 256
Gln Phe His Thr Glu Asp Tyr Phe Gly Lys Glu Ser Leu Trp Thr Gly
2565 2570 2575
Lys Gly Ile Gln Leu Ala Asp Gly Gly Trp Leu Ile Pro Ser Asn Asp
2580 2585 2590
Gly Lys Ala Gly Lys Glu Glu Phe Tyr Arg Ala Leu Cys Asp Thr Pro
2595 2600 2605
Gly Val Asp Pro Lys Leu Ile Ser Arg Ile Trp Val Tyr Asn His Tyr
2610 2615 2620
Arg Trp Ile Ile Trp Lys Leu Ala Ala Met Glu Cys Ala Phe Pro Lys
2625 2630 2635 264
Glu Phe Ala Asn Arg Cys Leu Ser Pro Glu Arg Val Leu Leu Gln Leu
2645 2650 2655
Lys Tyr Arg Tyr Asp Thr Glu Ile Asp Arg Ser Arg Arg Ser Ala Ile
2660 2665 2670
Lys Lys Ile Met Glu Arg Asp Asp Thr Ala Ala Lys Thr Leu Val Leu
2675 2680 2685
Cys Val Ser Asp Ile Ile Ser Leu Ser Ala Asn Ile Ser Glu Thr Ser
2690 2695 2700
Ser Asn Lys Thr Ser Ser Ala Asp Thr Gln Lys Val Ala Ile Ile Glu
2705 2710 2715 272
Leu Thr Asp Gly Trp Tyr Ala Val Lys Ala Gln Leu Asp Pro Pro Leu
2725 2730 2735
Leu Ala Val Leu Lys Asn Gly Arg Leu Thr Val Gly Gln Lys Ile Ile

2740 2745 2750

Leu His Gly Ala Glu Leu Val Gly Ser Pro Asp Ala Cys Thr Pro Leu
2755 2760 2765

Glu Ala Pro Glu Ser Leu Met Leu Lys Ile Ser Ala Asn Ser Thr Arg
2770 2775 2780

Pro Ala Arg Trp Tyr Thr Lys Leu Gly Phe Phe Pro Asp Pro Arg Pro
2785 2790 2795 280

Phe Pro Leu Pro Leu Ser Ser Leu Phe Ser Asp Gly Gly Asn Val Gly
2805 2810 2815

Cys Val Asp Val Ile Ile Gln Arg Ala Tyr Pro Ile Gln Trp Met Glu
2820 2825 2830

Lys Thr Ser Ser Gly Leu Tyr Ile Phe Arg Asn Glu Arg Glu Glu Glu
2835 2840 2845

Lys Glu Ala Ala Lys Tyr Val Glu Ala Gln Gln Lys Arg Leu Glu Ala
2850 2855 2860

Leu Phe Thr Lys Ile Gln Glu Glu Phe Glu Glu His Glu Glu Asn Thr
2865 2870 2875 288

Thr Lys Pro Tyr Leu Pro Ser Arg Ala Leu Thr Arg Gln Gln Val Arg
2885 2890 2895

Ala Leu Gln Asp Gly Ala Glu Leu Tyr Glu Ala Val Lys Asn Ala Ala
2900 2905 2910

Asp Pro Ala Tyr Leu Glu Gly Tyr Phe Ser Glu Glu Gln Leu Arg Ala
2915 2920 2925

Leu Asn Asn His Arg Gln Met Leu Asn Asp Lys Lys Gln Ala Gln Ile
2930 2935 2940

Gln Leu Glu Ile Arg Lys Thr Met Glu Ser Ala Glu Gln Lys Glu Gln
2945 2950 2955 296

Gly Leu Ser Arg Asp Val Thr Thr Val Trp Lys Leu Arg Ile Val Ser
2965 2970 2975

Tyr Ser Lys Lys Glu Lys Asp Ser Val Ile Leu Ser Ile Trp Arg Pro
2980 2985 2990

Ser Ser Asp Leu Tyr Ser Leu Leu Thr Glu Gly Lys Arg Tyr Arg Ile
2995 3000 3005

Tyr His Leu Ala Thr Ser Lys Ser Lys Ser Lys Ser Glu Arg Ala Asn
3010 3015 3020

Ile Gln Leu Ala Ala Thr Lys Lys Thr Gln Tyr Gln Gln Leu Pro Val
3025 3030 3035 304

Ser Asp Glu Ile Leu Phe Gln Ile Tyr Gln Pro Arg Glu Pro Leu His
3045 3050 3055

Phe Ser Lys Phe Leu Asp Pro Asp Phe Gln Pro Ser Cys Ser Glu Val
3060 3065 3070

Asp Leu Ile Gly Phe Val Val Ser Val Val Lys Lys Thr Gly Leu Ala
3075 3080 3085

Pro Phe Val Tyr Leu Ser Asp Glu Cys Tyr Asn Leu Leu Ala Ile Lys
3090 3095 3100

Phe Trp Ile Asp Leu Asn Glu Asp Ile Ile Lys Pro His Met Leu Ile
3105 3110 3115 312

Ala Ala Ser Asn Leu Gln Trp Arg Pro Glu Ser Lys Ser Gly Leu Leu
3125 3130 3135

Thr Leu Phe Ala Gly Asp Phe Ser Val Phe Ser Ala Ser Pro Lys Glu
3140 3145 3150

Gly His Phe Gln Glu Thr Phe Asn Lys Met Lys Asn Thr Val Glu Asn
3155 3160 3165

Ile Asp Ile Leu Cys Asn Glu Ala Glu Asn Lys Leu Met His Ile Leu
3170 3175 3180

His Ala Asn Asp Pro Lys Trp Ser Thr Pro Thr Lys Asp Cys Thr Ser
3185 3190 3195 320

Gly Pro Tyr Thr Ala Gln Ile Ile Pro Gly Thr Gly Asn Lys Leu Leu
3205 3210 3215

Met Ser Ser Pro Asn Cys Glu Ile Tyr Tyr Gln Ser Pro Leu Ser Leu
3220 3225 3230

Cys Met Ala Lys Arg Lys Ser Val Ser Thr Pro Val Ser Ala Gln Met
3235 3240 3245
Thr Ser Lys Ser Cys Lys Gly Glu Lys Glu Ile Asp Asp Gln Lys Asn
3250 3255 3260
Cys Lys Lys Arg Arg Ala Leu Asp Phe Leu Ser Arg Leu Pro Leu Pro
3265 3270 3275 328
Pro Pro Val Ser Pro Ile Cys Thr Phe Val Ser Pro Ala Ala Gln Lys
3285 3290 3295
Ala Phe Gln Pro Pro Arg Ser Cys Gly Thr Lys Tyr Glu Thr Pro Ile
3300 3305 3310
Lys Lys Lys Glu Leu Asn Ser Pro Gln Met Thr Pro Phe Lys Lys Phe
3315 3320 3325
Asn Glu Ile Ser Leu Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu
3330 3335 3340
Ala Leu Ile Asn Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys
3345 3350 3355 336
Gln Phe Ile Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser
3365 3370 3375
Glu Asp Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys
3380 3385 3390
Glu Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys
3395 3400 3405
Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile
3410 3415

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 2F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

TGAGTTTTAC CTCAGTCACA 20

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 41 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

CAGGAAACAG CTATGACCCT GTGACGTACT GGGTTTTTAG C 41

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 3FII primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

GATCTTTAAC TGTTCTGGGT CACA 24

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 3RII primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

CCCAGCATGA CACAATTAAT GA 22

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 44 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 4F/M 13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

TGTAAAACGA CGGCCAGTAG AATGCAAATT TATAATCCAG AGTA 44

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 4R-1A primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

ATCAGATTCA TCTTTATAGA AC 22

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 5+6F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

TGTAAAACGA CGGCCAGTTG TGTTGGCATT TTAAACATCA 40

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 38 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 5+6R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

CAGGAAACAG CTATGACCCA GGGCAAAGGT ATAACGCT 38

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 38 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 7F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

TGTAAAACGA CGGCCAGTTA AGTGAAATAA AGAGTGAA 38

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 7R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

CAGGAAACAG CTATGACCAG AAGTATTAGA GATGAC 36

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 8F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

TGTAAAACGA CGGCCAGTGC CATATCTTAC CACCTTGTGA 40

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 8FIA primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

TTGCATTCTA GTGATAATAT AC 22

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 8RIA primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

AATTGTTAGC AATTTCAAC 19

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 9F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

TGTAAAACGA CGGCCAGTTG GACCTAGGTT GATTGCAGAT 40

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 9R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

CAGGAAACAG CTATGACCTA AACTGAGATC ACGGGTGACA 40

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 10AF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

GAATAATATA AATTATATGG CTTA 24

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 37 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:

(D) OTHER INFORMATION: 10AR/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

CAGGAAACAG CTATGACCCC TAGTCTTGCT AGTTCTT 37

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 42 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 10BF/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

TGTAAAACGA CGGCCAGTAR CTGAAGTGGA ACCAAATGAT AC 42

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 44 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 10BR/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

CAGGAAACAG CTATGACCAC GTGGCAAAGA ATTCTCTGAA GTAA 44

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 10CF/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

TGTAAAACGA CGGCCAGTCA GCATCTTGAA TCTCATACAG 40

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 10CRII primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

AGACAGAGGT ACCTGAATC 19

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11AF-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

TGTAAAACGA CGGCCAGTTG GTACTTTAAT TTTGTCACTT 40

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 37 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11AR-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

CAGGAAACAG CTATGACCTG CAGGCATGAC AGAGAAT 37

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11BF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

AAGAAGCAAA ATGTAATAAG GA 22

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11BR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

CATTTAAAGC ACATACATCT TG 22

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11CF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

TCTAGAGGCA AAGAATCATA C 21

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11CR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

CAAGATTATT CCTTTCATTA GC 22

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11DF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

AACCAAAACA CAAATCTAAG AG 22

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11DR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

GTCATTTTTA TATGCTGCTT TAC 23

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11EF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

GGTTTTATAT GGAGACACAG G 21

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11ER primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

GTATTTACAA TTTCAACACA AGC 23

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11FF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

ATCACAGTTT TGGAGGTAGC 20

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11FR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

CTGACTTCCT GATTCTTCTA A 21

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11GF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

CTCAGATGTT ATTTTCCAAG C 21

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11GR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

CTGTTAAATA ACCAGAAGCA C 21

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11HF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

AGGTAGACAG CAGCAAGC 18

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: None
(B) LOCATION:
(D) OTHER INFORMATION: 11HR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

GTAATATCAG TTGGCATTTA TT 22

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11IF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

TGCAGAGGTA CATCCAATAA G 21

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11IR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

GATCAGTAAA TAGCAAGTCC G 21

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11JF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

TACTGAAAAT GAAGATAACA AAT 23

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: !!JR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

ATTTTGTTCT TTCTTATGTC AG 22

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:

(D) OTHER INFORMATION: 11KF-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

TGTAAAACGA CGGCCAGTCT ACTAAAACGG AGCAA 35

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11KR-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

CAGGAAACAG CTATGACCGT ATGAAAACCC AACAG 35

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11LF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

CACAAAATAC TGAAAGAAAG TG 22

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11LR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

GGCACCACAG TCTCAATAG 19

(2) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11MF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

GCAAAGACCC TAAAGTACAG 20

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11MR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

CATCAAATAT TCCTTCTCTA AG 22

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11NF-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

TGTAAAACGA CGGCCAGTGA AAATTCAGCC TTAGC 35

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11NR-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

CAGGAAACAG CTATGACCAT CAGAATGGTA GGAAT 35

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11OF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

GTACTATAGC TGAAAATGAC AA 22

(2) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11OR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

ACCACTGGCT ATCCTAAATG 20

(2) INFORMATION FOR SEQ ID NO:66:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11PF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

TGAAGATATT TGCGTTGAGG 20

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11PR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

GTCAGCAAAA ACCTTATGTG 20

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11QF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

ACGAAAATTA TGGCAGGTTG T 21

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11QR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

CTTGTCTTGC GTTTTGTAAT G 21

(2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11RF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

GCTTCATAAG TCAGTCTCAT 20

(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11RR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

TCAAATTCCT CTAACACTCC 20

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11SF-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

TGTAAAACGA CGGCCAGTTA CAGCAAGTGG AAAGC 35

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 37 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11SR-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

CAGGAAACAG CTATGACCAA GTTTCAGTTT TACCAAT 37

(2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:

(B) LOCATION:
(D) OTHER INFORMATION: 11TF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

GTTCTTCAGA AAATAATCAC TC 22

(2) INFORMATION FOR SEQ ID NO:75:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11TR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

TGTAAAAAGA GAATGTGTGG C 21

(2) INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 39 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11UF-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

TGTAAAACGA CGGCCAGTAC TTTTTCTGAT GTTCCTGTG 39

(2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 39 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 11UR-M13 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

CAGGAAACAG CTATGACCTA AAAATAGTGA TTGGCAACA 39

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 42 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 12F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

TGTAAAACGA CGGCCAGTAG TGGTGTTTTA AAGTGGTCAA AA 42

(2) INFORMATION FOR SEQ ID NO:79:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 12R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

CAGGAAACAG CTATGACCGG ATCCACCTGA GGTCAGAATA 40

(2) INFORMATION FOR SEQ ID NO:80:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 13-2F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

TAACATTTAA GCATCCGTTA C 21

(2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 13-2R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

AAACGAGACT TTTCTCATAC TGTATTAG 28

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 14F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

ACCATGTAGC AAATGAGGGT CT 22

(2) INFORMATION FOR SEQ ID NO:83:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 14AR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

GCTTTTGTCT GTTTTCCTCC AA 22

(2) INFORMATION FOR SEQ ID NO:84:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 15-2F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

CCAGGGGTTG TGCTTTTTAA A 21

(2) INFORMATION FOR SEQ ID NO:85:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 38 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 15FUT/M13-R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

CAGGAAACAG CTATGACCAC TCTGTCATAA AAGCCATC 38

(2) INFORMATION FOR SEQ ID NO:86:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 16AF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

TTTGGTTTGT TATAATTGTT TTTA 24

(2) INFORMATION FOR SEQ ID NO:87:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 16AR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

CCAACTTTTT AGTTCGAGAG 20

(2) INFORMATION FOR SEQ ID NO:88:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 17F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

TTCAGTATCA TCCTATGTG 19

(2) INFORMATION FOR SEQ ID NO:89:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 17AR primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

AGAAACCTTA ACCCATACTG 20

(2) INFORMATION FOR SEQ ID NO:90:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 39 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 18FUT/M13-AF primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

TGTAAAACGA CGGCCAGTGA ATTCTAGAGT CACACTTCC 39

(2) INFORMATION FOR SEQ ID NO:91:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 38 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 18R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

CAGGAAACAG CTATGACCTT TAACTGAATC AATGACTG 38

(2) INFORMATION FOR SEQ ID NO:92:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 41 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 19F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

TGTAAAACGA CGGCCAGTAA GTGAATATTT TTAAGGCAGT T 41

(2) INFORMATION FOR SEQ ID NO:93:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 39 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 19FUT/M13-R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

CAGGAAACAG CTATGACCAA GAGACCGAAA CTCCATCTC 39

(2) INFORMATION FOR SEQ ID NO:94:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 38 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 20F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

TGTAAAACGA CGGCCAGTCA CTGTGCCTGG CCTGATAC 38

(2) INFORMATION FOR SEQ ID NO:95:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 39 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 20R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

CAGGAAACAG CTATGACCAT GTTAAATTCA AAGTCTCTA 39

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 39 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 21F/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

TGTAAAACGA CGGCCAGTGG GTGTTTTATG CTTGGTTCT 39

(2) INFORMATION FOR SEQ ID NO:97:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 21R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

CAGGAAACAG CTATGACCCA TTTCAACATA TTCCTTCCTG 40

(2) INFORMATION FOR SEQ ID NO:98:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 22F-1A primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

AACCACACCC TTAAGATGA 19

(2) INFORMATION FOR SEQ ID NO:99:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 22R-1A primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

GCATTAGTAG TGGATTTTGC 20

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 16 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 23FII primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

TCACTTCCAT TGCATC 16

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 23RII primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

TGCCAACTGG TAGCTCC 17

(2) INFORMATION FOR SEQ ID NO:102:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 24 2F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

TACAGTTAGC AGCGACAAAA 20

(2) INFORMATION FOR SEQ ID NO:103:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 38 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 24R/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

CAGGAAACAG CTATGACCAT TTGCCAACTG GTAGCTCC 38

(2) INFORMATION FOR SEQ ID NO:104:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 25F-7/23 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

GCTTTCGCCA AATTCAGCTA 20

(2) INFORMATION FOR SEQ ID NO:105:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 25R-7/23 primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

TACCAAAATG TGTGGTGATG 20

(2) INFORMATION FOR SEQ ID NO:106:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 26-2F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

AATCACTGAT ACTGGTTTTG 20

(2) INFORMATION FOR SEQ ID NO:107:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 26-2R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

TATACTTACA GGAGCCACAT 20

(2) INFORMATION FOR SEQ ID NO:108:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 27AF-1A primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

CTGTGTGTAA TATTTGCG 18

(2) INFORMATION FOR SEQ ID NO:109:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 27AR/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

CAGGAAACAG CTATGACGGC AAGTTCTTCG TCAGCTATTG 40

(2) INFORMATION FOR SEQ ID NO:110:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 27BF/M13F primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

TGTAAAACGA CGGCCAGTGA ATTCTCCTCA GATGACTCCA 40

(2) INFORMATION FOR SEQ ID NO:111:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 38 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(A) NAME/KEY:
(B) LOCATION:
(D) OTHER INFORMATION: 27BR/M13R primer

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

CAGGAAACAG CTATGACCTC TTTGCTCATT GTGCAACA 38

WE CLAIM:

1. A genomic DNA containing a BRCA2 gene,

wherein the first twelve nucleotides beginning exon 5 are 5'-TCCTGTTGTTCT-3' as set forth in SEQ. ID. NO: 1,

wherein nucleotides numbers 5782-5790 are GTTTGTGTT as set forth in SEQ. ID. NO: 4, and

wherein the last 20 nucleotides ending exon 15 are 5'-CTGCGTGTTCTCATAAACAG-3' as set forth in SEQ. ID. NO: 2 and the first 20 nucleotides beginning exon 16 are 5'-CTGTATACGTATGGCGTTTC-3' as set forth in SEQ. ID. NO: 3.

2. The genomic DNA according to claim 1 wherein the coding sequence nucleotides are as follows:

1093 A
1342 A
1593 A
2457 T
2908 G
3199 A
3624 A
4035 T
7470 A
9079 G.

3. The genomic DNA according to claim 1 wherein the coding sequence nucleotides are as follows:

1093 A
1342 C
1593 A
2457 T
2908 G
3199 A
3624 A
4035 T
7470 A
9079 G.

4. The genomic DNA according to claim 1 wherein the coding sequence nucleotides are as follows:

1093 A
1342 C
1593 A
2457 T
2908 G
3199 A
3624 A
4035 C
7470 A
9079 G.

5. The genomic DNA according to claim 1 wherein the coding sequence nucleotides are as follows:

1093 C
1342 A
1593 A
2457 C
2908 G
3199 G
3624 G
4035 T
7470 G
9079 G.

6. The genomic DNA according to claim 1 wherein the coding sequence nucleotides are as follows:

1093 A
1342 C
1593 A
2457 T
2908 G
3199 A
3624 G
4035 T
7470 G
9079 G.

7. The genomic DNA according to claim 1 wherein the coding sequence nucleotides are as follows:

1093 C
1342 C
1593 G
2457 C
2908 A
3199 G

3624 A
4035 T
7470 A
9079 A.

8. The genomic DNA according to claim 1 wherein the coding sequence nucleotides are as follows:

2024 C
4553 C
4815 G
5841 T
5972 C.

9. A DNA comprising a BRCA2 coding sequence,
wherein nucleotide numbers 643-666 are CTTAGTGAAAGTCCTGTTGTTCTA and
wherein nucleotides numbers 5782-5790 are GTTTGTGTT.

10. The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

1093 A
1342 A
1593 A
2457 T
2908 G
3199 A
3624 A
4035 T
7470 A
9079 G.

11. The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

1093 A
1342 C
1593 A
2457 T
2908 G
3199 A
3624 A
4035 T
7470 A
9079 G

as set forth in SEQ. ID. NO: 4.

12. The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

1093 A
1342 C
1593 A
2457 T
2908 G
3199 A
3624 A
4035 C
7470 A
9079 G

as set forth in SEQ. ID. NO: 6.

13. The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

1093 C
1342 A
1593 A
2457 C
2908 G
3199 G
3624 G
4035 T
7470 G
9079 G

as set forth in SEQ. ID. NO: 8.

14. The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

1093 A
1342 C
1593 A
2457 T
2908 G
3199 A
3624 G
4035 T
7470 G
9079 G

as set forth in SEQ. ID. NO: 10.

15. The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

1093 C
1342 C
1593 G
2457 C

2908 A
3199 G
3624 A
4035 T
7470 A
9079 A

as set forth in SEQ. ID. NO: 12.

16. The DNA according to claim 9 wherein the coding sequence nucleotides are as follows:

2024 C
4553 C
4815 G
5841 T
5972 C.

17. A BRCA2 protein having the following amino acids at the following peptide numbers:

289 asparagine
372 histidine
894 valine
991 asparagine
1852 valine
1853 cysteine
1854 valine
2951 alanine

as set forth in SEQ. ID. NO: 5.

18. The BRCA2 protein having the following amino acids at the following peptide numbers:

289 asparagine
372 asparagine
599 serine
894 valine
991 asparagine
2951 alanine.

19. The BRCA2 protein having the following amino acids at the following peptide numbers:

289 histidine
372 histidine
894 valine
991 asparatic acid
2951 alanine

as set forth in SEQ. ID. NO: 9.

20. The BRCA2 protein having the following amino acids at the following peptide numbers:

289 histidine
372 asparagine
894 isoleucine
991 aspartic acid
2951 threonine

as set forth in SEQ. ID. NO: 13.

21. The BRCA2 protein according to claims 17-20 having the following amino acids at the following peptide numbers:

599 serine
1442 serine
1915 threonine.

22. A haplotype of BRCA2 coding sequence ($BRCA2^{omi\ 1}$) as set forth in SEQ. ID. NO: 4 or a sequence complementary thereto.

23. A BRCA2 protein comprising an amino acid sequence derived from $BRCA2^{omi\ 1}$ as set forth in SEQ. ID. NO: 5.

24. A haplotype of BRCA2 coding sequence ($BRCA2^{omi\ 2}$) as set forth in SEQ. ID. NO: 6 or a sequence complementary thereto.

25. A BRCA2 protein comprising an amino acid sequence derived from $BRCA2^{omi\ 2}$ as set forth in SEQ. ID. NO: 7.

26. A haplotype of BRCA2 coding sequence ($BRCA2^{omi\ 3}$) as set forth in SEQ. ID. NO: 8 or a sequence complementary thereto.

27. A BRCA2 protein comprising an amino acid sequence derived from $BRCA2^{omi\ 3}$ as set forth in SEQ. ID. NO: 9.

28. A haplotype of BRCA2 coding sequence ($BRCA2^{omi\ 4}$) as set forth in SEQ. ID. NO: 10 or a sequence complementary thereto.

29. A BRCA2 protein comprising an amino acid sequence derived from $BRCA2^{omi\ 4}$ as set forth in SEQ. ID. NO: 11.

30. A haplotype of BRCA2 coding sequence ($BRCA2^{omi\ 5}$) as set forth in SEQ. ID. NO: 12 or a sequence complementary thereto.

31. A BRCA2 protein comprising an amino acid sequence derived from $BRCA2^{omi\ 5}$ as set forth in SEQ. ID. NO: 13.

32. A method of identifying individuals having a BRCA2 gene with a BRCA2 coding sequence not associated with disease, comprising:

(a) amplifying a DNA or a fragment thereof of an individual's BRCA2 coding sequence;

(b) sequencing said amplified DNA fragment;

(c) if necessary, repeating steps (a) and (b) until said individual's BRCA2 coding sequence is sufficiently sequenced to determine whether a mutation is present;

(d) comparing the sequence of said amplified DNA fragment to a $BRCA2^{(omi)}$ DNA sequence selecting from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences;

(e) determining the presence of absence of each of the following polymorphic variations in said individual's BRCA2 coding sequence:

(i) AAT and CAT at position 1093,

(ii) CAT and AAT at position 1342,

(iii) TCA and TCG at position 1593,

(iv) CAT and CAC at position 2457,

(v) GTA and ATA at position 2908,

(vi) AAC and GAC at position 3199,

(vii) AAA and AAG at position 3624,

(viii) GTT and GTC at position 4035,

(ix) TCA and TCG at position 7470, and

(x) GCC and ACC at position 9079; and

(f) determining any sequence differences between said individual's BRCA2 coding sequences and a BRCA2$^{(omi)}$ DNA sequence selected from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences, wherein the presence of said polymorphic variations and the absence of a variation outside of positions 1093, 1342, 1593, 2457, 2908, 3199, 3624, 4035, 7470, and 9079 is correlated with an absence of increased genetic susceptibility to breast or ovarian cancer resulting from a BRCA2 mutation in the BRCA2 coding sequence.

33. A method of identifying individuals having a BRCA2 gene with a BRCA2 coding sequence not associated with disease, comprising:

(a) amplifying a DNA or a fragment thereof of an individual's BRCA2 coding sequence;

(b) sequencing said amplified DNA fragment;

(c) if necessary, repeating steps (a) and (b) until said individual's BRCA2 coding sequence is sufficiently sequenced to determine whether a mutation is present;

(d) comparing the sequence of said amplified DNA fragment to a BRCA2$^{(omi)}$ DNA sequence selecting from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences;

(e) determining the presence of absence of each of the following polymorphic variations in said individual's BRCA2 coding sequence:

(i) AAT and CAT at position 1093,

(ii) CAT and AAT at position 1342,

(iii) TCA and TCG at position 1593,

(iv) CAT and CAC at position 2457,

(v) GTA and ATA at position 2908,

(vi) AAC and GAC at position 3199,

(vii) AAA and AAG at position 3624,

(viii) GTT and GTC at position 4035,

(ix) TCA and TCG at position 7470, and

(x) GCC and ACC at position 9079; and

(f) determining any sequence differences between said individual's BRCA2 coding sequences and a BRCA2$^{(omi)}$ DNA sequence selected from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences, wherein the presence of said polymorphic variations and the absence of a variation outside of positions 1093, 1342, 1593, 2457, 2908, 3199, 3624, 4035, 7470, and 9079 is correlated with an absence of increased genetic susceptibility to breast or ovarian cancer resulting from a BRCA2 mutation in the BRCA2 coding sequence; wherein, codon variations occur at the following frequencies, respectively, in a Caucasian population of individuals free of disease:

(i) at position 1093, AAT and CAT occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(ii) at position 1342, CAT and AAT occur at frequencies from about 35-45%, and from about 55-65%, respectively,

(iii) at position 1593, TCA and TCG occur at frequencies from about 85-95%, and from about 5-15%, respectively,

(iv) at position 2457, CAT and CAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(v) at position 2908, GTA and ATA occur at frequencies from about 85-95%, and from about 5-15%, respectively,

(vi) at position 3199, AAC and GAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(vii) at position 3624, AAA and AAG occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(viii) at position 4035, GTT and GTC occur at frequencies from about 85-95%, and from about 5-15%, respectively,

(ix) at position 7470, TCA and TCG occur at frequencies from about 75-85%, and from about 15-25%, respectively, and

(x) at position 9079, GCC and ACC occur at frequencies from about 85-95%, and from about 5-15%, respectively.

34. A method of detecting an increased genetic susceptibility to breast and ovarian cancer in an individual resulting from the presence of a mutation in the BRCA2 coding sequence, comprising:

(a) amplifying a DNA or a fragment thereof of an individual's BRCA2 coding sequence;

(b) sequencing said amplified DNA fragment;

(c) if necessary, repeating steps (a) and (b) until said individual's BRCA2 coding sequence is sufficiently sequenced to determine whether a mutation is present;

(d) comparing the sequence of said amplified DNA fragment to a $BRCA2^{(omi)}$ DNA sequence selected from the group consisting of SEQ.

ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences;

(e) determining any sequence differences between said individual's BRCA2 coding sequences and a BRCA2$^{(omi)}$ DNA sequence selected from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences in order to determine the presence or absence of base changes in said individual's BRCA2 coding sequence wherein a base change which is not any one of the following:

(i) AAT and CAT at position 1093,

(ii) CAT and AAT at position 1342,

(iii) TCA and TCG at position 1593,

(iv) CAT and CAC at position 2457,

(v) GTA and ATA at position 2908,

(vi) AAC and GAC at position 3199,

(vii) AAA and AAG at position 3624,

(viii) GTT and GTC at position 4035,

(ix) TCA and TCG at position 7470, and

(x) GCC and ACC at position 9079, is correlated with the potential of increased genetic susceptibility to breast or ovarian cancer resulting from a BRCA2 mutation in the BRCA2 coding sequence.

35. A method of detecting an increased genetic susceptibility to breast and ovarian cancer in an individual resulting from the presence of a mutation in the BRCA2 coding sequence, comprising:

(a) amplifying a DNA or a fragment thereof of an individual's BRCA2 coding sequence;

(b) sequencing said amplified DNA fragment;

(c) if necessary, repeating steps (a) and (b) until said individual's BRCA2 coding sequence is sufficiently sequenced to determine whether a mutation is present;

(d) comparing the sequence of said amplified DNA fragment to a $BRCA2^{(omi)}$ DNA sequence selected from the group consisting of: SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences;

(e) determining any sequence differences between said individual's BRCA2 coding sequences and a $BRCA2^{(omi)}$ DNA sequence selected from the group consisting of: SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, and their respective complementary sequences in order to determine the presence or absence of base changes in said individual's BRCA2 coding sequence wherein a base change which is not any one of the following:

(i) AAT and CAT at position 1093,

(ii) CAT and AAT at position 1342,

(iii) TCA and TCG at position 1593,

(iv) CAT and CAC at position 2457,

(v) GTA and ATA at position 2908,

(vi) AAC and GAC at position 3199,

(vii) AAA and AAG at position 3624,

(viii) GTT and GTC at position 4035,

(ix) TCA and TCG at position 7470, and

(x) GCC and ACC at position 9079, is correlated with the potential of increased genetic susceptibility to breast or ovarian cancer resulting from a BRCA2 mutation in the BRCA2 coding sequence, wherein, codon variations occur at the following frequencies, respectively, in a Caucasian population of individuals free of disease:

(i) at position 1093, AAT and CAT occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(ii) at position 1342, CAT and AAT occur at frequencies from about 35-45%, and from about 55-65%, respectively,

(iii) at position 1593, TCA and TCG occur at frequencies from about 85-95%, and from about 5-15%, respectively,

(iv) at position 2457, CAT and CAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(v) at position 2908, GTA and ATA occur at frequencies from about 85-95%, and from about 5-15%, respectively,

(vi) at position 3199, AAC and GAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(vii) at position 3624, AAA and AAG occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(viii) at position 4035, GTT and GTC occur at frequencies from about 85-95%, and from about 5-15%, respectively,

(ix) at position 7470, TCA and TCG occur at frequencies from about 75-85%, and from about 15-25%, respectively, and

(x) at position 9079, GCC and ACC occur at frequencies from about 85-95%, and from about 5-15%, respectively.

36. A method according to any of the claims 32-35 wherein the said amplifying is performed by annealing at least one oligonucleotide primer to said DNA fragment and extending the oligonucleotide primer by an agent for polymerization.

37. A method according to claim 36 wherein said oligonucleotide primer is directly or indirectly labeled with a radioactive label, a fluorescent label, a bioluminescent label, a chemiluminescent label, a metal chelator, or an enzyme label.

38. A BRCA2 coding sequence according to claims 32, wherein the codon pairs occur at the following frequencies:

(i) at position 1093, AAT and CAT occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(ii) at position 1342, CAT and AAT occur at frequencies from about 35-45%, and from about 55-65%, respectively,

(iii) at position 1593, TCA and TCG occur at frequencies from about 85-95%, and from about 5-15%, respectively,

(iv) at position 2457, CAT and CAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(v) at position 2908, GTA and ATA occur at frequencies from about 85-95%, and from about 5-15%, respectively,

(vi) at position 3199, AAC and GAC occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(vii) at position 3624, AAA and AAG occur at frequencies from about 75-85%, and from about 15-25%, respectively,

(viii) at position 4035, GTT and GTC occur at frequencies from about 85-95%, and from about 5-15%, respectively,

(ix) at position 7470, TCA and TCG occur at frequencies from about 75-85%, and from about 15-25%, respectively, and

(x) at position 9079, GCC and ACC occur at frequencies from about 85-95%, and from about 5-15%, respectively.

39. An oligonucleotide primer capable of hybridizing to a sample of BRCA2 gene, or its respective complementary sequences selected from the group consisting of SEQ. ID. NO: 14, 19, 22, 23, 25, 26, 29-76, 83, 85-88, 90, 91, 97, 98, 101, and 104-107.

40. A chip array having "n" elements for performing allele specific sequence-based techniques comprising a solid phase chip and oligonucleotides having "n" different nucleotide sequences,

wherein "n" is an interger greater than or equal to ten,

wherein said oligonucleotides are bound to said solid phase chip in a manner which permits said oligonucleotides to effectively hybridize to complementary oligonucleotides or polynucleotides,

wherein oligonucleotides having different nucleotide sequence are bound to said solid phase chip at different locations so that a particular location on said solid phase chip exclusively binds oligonucleotides having a specific nucleotide sequence, and

wherein at least ten oligonucleotides are capable of specifically hybridizing to the BRCA2 DNA having the sequence as set forth in SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12 or their respective complementary sequences, at least one oligonucleotide being capable of specifically hybridizing at each of the nucleotide positions 1093, 1342, 1593, 2457, 2908, 3199, 3624, 4035, 7470, 9079, or complementary thereto.

41. A method of performing gene therapy on a patient, comprising:

a) contacting cancer cells *in vivo* with an effective amount of a vector comprising DNA containing at least a portion of BRCA2 sequence selected from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, or their respective complementary sequences

b) allowing the vector to enter the cancer cells, and

c) measuring a reduction in tumor growth.

42. The method according to claim 41 wherein said cancer cells have a mutation in the BRCA2 gene.

43. The method according to claim 41 wherein said patient has a mutation in the BRCA2 gene of non-cancer cells.

44. A method of performing gene therapy on a patient or a sample, comprising:

a) contacting cells *in vivo* or *in vitro* with an effective amount of a vector comprising DNA containing at least a portion of BRCA2 sequence selected from the group consisting of SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, or their respective complementary sequences, and

b) allowing the vector to enter the cells,

wherein said patient has a reduced susceptibility for developing a cancer associated with a mutation in the BRCA2 gene.

45. A method according to claim 44 wherein said cells include healthy breast, ovarian or pancreatic tissues.

46. A method according to claim 44 wherein a patient has an inherited mutation in the BRCA2 gene.

47. A method of treating a patient suspected of having a tumor, comprising:

a) administering to a patient an effective amount of BRCA2 tumor growth inhibitor having an amino acid sequence selected from the group consisting of SEQ. ID. NO: 5, SEQ. ID. NO: 7, SEQ. ID. NO: 9, SEQ. ID. NO: 11, SEQ. ID. NO: 13, any fragments thereto, and any functional equivalent thereof;

b) allowing the patient's cells to take up the protein, and

c) measuring a reduction in tumor growth.

48. The method according to claim 47 wherein said tumor is a breast cancer, an ovarian cancer or a pancreatic cancer.

49. The method according to claim 47 wherein said patient has an inherited mutation in the BRCA2 gene.

50. A method of preventing the formation or growth of a tumor, comprising:

a) adminstering to a patient an effective amount of BRCA2 tumor growth inhibiting protein having an amino acid sequence selected from the group consisting of SEQ. ID. NO: 5, SEQ. ID. NO: 7, SEQ. ID. NO: 9, SEQ. ID. NO: 11, SEQ. ID. NO: 13, any fragments thereto, and any functional equivalent thereof; and

b) allowing the patient cells to take up the protein.

51. The method according to claim 31 wherein the protein is administered parenternally, by buccal adsorption or inhalation.

52. A cloning vector comprising:

(a) a DNA sequence as set forth in SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, or any fragments thereof; and

(b) one or more suitable regulatory sequences to induce replication and/or integration in a host cell.

53. An expression vector comprising a DNA sequence as set forth in SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, or any fragments thereof operatively linked to one or more promoter sequences capable of directing expression of said sequence in a host cell.

54. A host cell transformed with the vector according to claim 52 or 53.

55. A BRCA2 polypeptide which is selected from the group consisting of:

(a) a fragment of BRCA2 protein sequence as set forth in SEQ. ID. NO: 5, SEQ. ID. NO: 7, SEQ. ID. NO: 9, SEQ. ID. NO: 11, or SEQ. ID. NO:13;

(b) an amino acid sequence which is substantially homologous to the BRCA2 protein sequence as set forth in SEQ. ID. NO: 5, SEQ. ID. NO: 7, SEQ. ID. NO: 9, SEQ. ID. NO: 11, or SEQ. ID. NO: 13;

(c) a molecule which has similar function to the BRCA2 protein; and

(d) a fusion protein of (a), (b), or (c).

56. An anti-BRCA2 antibody wherein a molecule according to claims 17-21, 23, 25, 27, 29, 31, or 55 is used as an immunogen.

57. A diagnostic reagent comprising a molecule selected from the group consisting of:
(a) a DNA sequence as set forth in SEQ. ID. NO: 4, SEQ. ID. NO: 6, SEQ. ID. NO: 8, SEQ. ID. NO: 10, SEQ. ID. NO: 12, or their complementary sequences;
(b) a nucleic acid fragment of (a) comprising at least 10 nucleotide in length;
(c) a sequence which hybridizes to (a) or (b);
(d) a polypeptide according to claim 17-21, 23, 25, 27, 29, 31, or 55; and
(e) an antibody which specifically binds to the polypeptide of (d).

58. A pharmaceutical composition comprising a molecule according to any one of the claims 17-21, 23, 25, 27, 29, 31, 55 in a pharmaceutically acceptable carrier.

59. A pharmaceutical composition comprising a molecule according claim 56 in a pharmaceutically acceptable carrier.

60. A pharmaceutical composition comprising a molecule according to claim 57 in a pharmaceutically acceptable carrier.

ABSTRACT OF THE DISCLOSURE

Five novel DNA and protein sequences have been determined for the BRCA2 gene, as have been ten polymorphic sites and their rates of occurrence in the normal alleles of BRCA2. The sequences $BRCA2^{(omi\ 1\text{-}5)}$ and the ten polymorphic sites will provide greater accuracy and reliability for genetic testing. One skilled in the art will be better able to avoid misinterpretations of changes in the gene and/or protein sequence, determine the presence of a normal sequence, and of mutations of BRCA2. This invention is also related to a method of performing gene therapy with $BRCA2^{(omi\ 1\text{-}5)}$ coding sequences or fragments thereof. This invention is further related to protein therapy with $BRCA2^{(omi\ 1\text{-}5)}$ proteins or their functional equivalents.

Figure 1A

Exon 2
taagtgcattttggtcttctgttttgcagACTTATTTACCAAGCATTGGAGGAATATCGTAGGTAAAA
ATGCCTATTGGATCCAAAGAGAGGCCAACATTTTTTGAAATTTTTAAGACACGCTGC
AACAAAGCAGgtattgacaaattttatataac

Exon 3
gggatttttttttaaatagATTTAGGACCAATAAGTCTTAATTGGTTTGAAGAACTTTCTTCAG
AAGCTCCACCCTATAATTCTGAACCTGCAGAAGAATCTGAACATAAAAACAACAATT
ACGAACCAAACCTATTTAAAACTCCACAAAGGAAACCATCTTATAATCAGCTGGCTT
CAACTCCAATAATATTCAAAGAGCAAGGGCTGACTCTGCCGCTGTACCAATCTCCT
GTAAAAGAATTAGATAAATTCAAATTAGACTTAGgtaagtaatgcaatatggtagactgggg

Exon 4
tcactgaattattgtactgtttcagGAAGGAATGTTCCCAATAGTAGACATAAAAGTCTTCGCACA
GTGAAAACTAAAATGGATCAAGCAGATGATGTTTCCTGTCCACTTCTAAATTCTTGT
CTTAGTGAAAGgtatgatgaagctattatattaaaa

Exon 5
agggatttgctttgt**TTTATTTTAG**TCCTGTTGTTCTACAATGTACACATGTAACACCACAAA
GAGATAAGTCAGgtatgattaaaaacaatgctttttattctt

Exon 6
ttaacaattttccccttttttttaccccccagTGGTATGTGGGAGTTTGTTTCATACACCAAAGTTTGTG
AAGgtaaatatt

Exon 7
taatgatcagggcatttctataaaaaataaactattttctttcctcccagGGTCGTCAGACACCAAAACATATT
TCTGAAAGTCTAGGAGCTGAGGTGGATCCTGATATGTCTTGGTCAAGTTCTTTAGC
TACACCACCCACCCTTAGTTCTACTGTGCTCATAGgtaataata

Exon 8
ttttatcttacagTCAGAAATGAAGAAGCATCTGAAACTGTATTTCCTCATGATACTACTGC
Tgtaagtaaatatgacattgattagact

Exon 9
taaactataatttttgcagAATGTGAAAAGCTATTTTTCCAATCATGATGAAAGTCTGAAGAAA
AATGATAGATTTATCGCTTCTGTGACAGACAGTGAAAACACAAATCAAAGAGAAGC
TGCAAGTCATGgtaagtcctct

Exon 10
ttaatgtgcttctgttttatactttaacagGATTTGGAAAAACATCAGGGAATTCATTTAAAGTAAATA
GCTGCAAAGACCACATTGGAAAGTCAATGCCAAATGTCCTAGAAGATGAAGTATAT
GAAACAGTTGTAGATACCTCTGAAGAAGATAGTTTTTCATTATGTTTTTCTAAATGTA
GAACAAAAAATCTACAAAAAGTAAGAACTAGCAAGACTAGGAAAAAAATTTTCCATG
AAGCAAACGCTGATGAATGTGAAAAATCTAAAAACCAAGTGAAAGAAAAATACTCAT
TTGTATCTGAAGTGGAACCAAATGATACTGATCCATTAGATTCAAATGTAGCAAATC

Figure 1B

AGAAGCCCTTTGAGAGTGGAAGTGACAAAATCTCCAAGGAAGTTGTACCGTCTTTG
GCCTGTGAATGGTCTCAACTAACCCTTTCAGGTCTAAATGGAGCCCAGATGGAGAA
AATACCCCTATTGCATATTTCTTCATGTGACCAAAATATTTCAGAAAAAGACCTATTA
GACACAGAGAACAAAAGAAAGAAAGATTTTCTTACTTCAGAGAATTCTTTGCCACGT
ATTTCTAGCCTACCAAAATCAGAGAAGCCATTAAATGAGGAAACAGTGGTAAATAA
GAGAGATGAAGAGCAGCATCTTGAATCTCATACAGACTGCATTCTTGCAGTAAAGC
AGGCAATATCTGGAACTTCTCCAGTGGCTTCTTCATTTCAGGGTATCAAAAAGTCTA
TATTCAGAATAAGAGAATCACCTAAAGAGACTTTCAATGCAAGTTTTTCAGGTCATA
TGACTGATCCAAACTTTAAAAAAGAAACTGAAGCCTCTGAAAGTGGACTGGAAATA
CATACTGTTTGCTCACAGAAGGAGGACTCCTTATGTCCAAATTTAATTGATAATGGA
AGCTGGCCAGCCACCACCACACAGAATTCTGTAGCTTTGAAGAATGCAGGTTTAAT
ATCCACTTTGAAAAAGAAAACAAATAAGTTTATTTATGCTATACATGATGAAACATCT
TATAAAGGAAAAAAAAATACCGAAAGACCAAAAATCAGAACTAATTAACTGTTCAGCC
CAGTTTGAAGCAAATGCTTTTGAAGCACCACTTACATTTGCAAATGCTGATTCAGgta
cctctgtct

Exon 11

tttgtgtttttatgtttagGTTTATTGCATTCTTCTGTGAAAAGAAGCTGTTCACAGAATGATTCT
GAAGAACCAACTTTGTCCTTAACTAGCTCTTTTGGGACAATTCTGAGGAAATGTTCT
AGAAATGAAACATGTTCTAATAATACAGTAATCTCTCAGGATCTTGATTATAAAGAA
GCAAAATGTAATAAGGAAAAACTACAGTTATTTATTACCCCAGAAGCTGATTCTCTG
TCATGCCTGCAGGAAGGACAGTGTGAAAATGATCCAAAAAGCAAAAAAGTTTCAGA
TATAAAAGAAGAGGTCTTGGCTGCAGCATGTCACCCAGTACAACATTCAAAAGTGG
AATACAGTGATACTGACTTTCAATCCCAGAAAAGTCTTTTATATGATCATGAAAATG
CCAGCACTCTTATTTTAACTCCTACTTCCAAGGATGTTCTGTCAAACCTAGTCATGA
TTTCTAGAGGCAAAGAATCATACAAAATGTCAGACAAGCTCAAAGGTAACAATTATG
AATCTGATGTTGAATTAACCAAAAATATTCCCATGGAAAAGAATCAAGATGTATGTG
CTTTAAATGAAAATTATAAAAACGTTGAGCTGTTGCCACCTGAAAAATACATGAGAG
TAGCATCACCTTCAAGAAAGGTACAATTCAACCAAAACACAAATCTAAGAGTAATCC
AAAAAAATCAAGAAGAAACTACTTCAATTTCAAAAATAACTGTCAATCCAGACTCTG
AAGAACTTTTCTCAGACAATGAGAATAATTTTGTCTTCCAAGTAGCTAATGAAAGGA
ATAATCTTGCTTTAGGAAATACTAAGGAACTTCATGAAACAGACTTGACTTGTGTAA
ACGAACCCATTTTCAAGAACTCTACCATGGTTTTATATGGAGACACAGGTGATAAAC
AAGCAACCCAAGTGTCAATTAAAAAAGATTTGGTTTATGTTCTTGCAGAGGAGAAC
AAAAATAGTGTAAAGCAGCATATAAAAATGACTCTAGGTCAAGATTTAAAATCGGAC
ATCTCCTTGAATATAGATAAAATACCAGAAAAAAATAATGATTACATGAACAAATGG
GCAGGACTCTTAGGTCCAATTTCAAATCACAGTTTTGGAGGTAGCTTCAGAACAGC
TTCAAATAAGGAAATCAAGCTCTCTGAACATAACATTAAGAAGAGCAAAATGTTCTT
CAAAGATATTGAAGAACAATATCCTACTAGTTTAGCTTGTGTTGAAATTGTAAATAC
CTTGGCATTAGATAATCAAAAGAAACTGAGCAAGCCTCAGTCAATTAATACTGTATC
TGCACATTTACAGAGTAGTGTAGTTGTTTCTGATTGTAAAAATAGTCATATAACCCC
TCAGATGTTATTTTCCAAGCAGGATTTTAATTCAAACCATAATTTAACACCTAGCCAA
AAGGCAGAAATTACAGAACTTTCTACTATATTAGAAGAATCAGGAAGTCAGTTTGAA
TTTACTCAGTTTAGAAAACCAAGCTACATATTGCAGAAGAGTACATTTGAAGTGCCT
GAAAACCAGATGACTATCTTAAAGACCACTTCTGAGGAATGCAGAGATGCTGATCT
TCATGTCATAATGAATGCCCCATCGATTGGTCAGGTAGACAGCAGCAAGCAATTTG

Figure 1C

AAGGTACAGTTGAAATTAAACGGAAGTTTGCTGGCCTGTTGAAAAATGACTGTAAC
AAAAGTGCTTCTGGTTATTTAACAGATGAAAATGAAGTGGGGTTTAGGGGCTTTTAT
TCTGCTCATGGCACAAAACTGAATGTTTCTACTGAAGCTCTGCAAAAAGCTGTGAA
ACTGTTTAGTGATATTGAGAATATTAGTGAGGAAACTTCTGCAGAGGTACATCCAAT
AAGTTTATCTTCAAGTAAATGTCATGATTCTGTTGTTTCAATGTTTAAGATAGAAAAT
CATAATGATAAAACTGTAAGTGAAAAAAATAATAAATGCCAACTGATATTACAAAATA
ATATTGAAATGACTACTGGCACTTTTGTTGAAGAAATTACTGAAAATTACAAGAGAA
ATACTGAAAATGAAGATAACAAATATACTGCTGCCAGTAGAAATTCTCATAACTTAG
AATTTGATGGCAGTGATTCAAGTAAAAATGATACTGTTTGTATTCATAAAGATGAAA
CGGACTTGCTATTTACTGATCAGCACAACATATGTCTTAAATTATCTGGCCAGTTTA
TGAAGGAGGGAAACACTCAGATTAAAGAAGATTTGTCAGATTTAACTTTTTTGGAAG
TTGCGAAAGCTCAAGAAGCATGTCATGGTAATACTTCAAATAAAGAACAGTTAACT
GCTACTAAAACGGAGCAAAATATAAAAGATTTTGAGACTTCTGATACATTTTTTCAG
ACTGCAAGTGGGAAAAATATTAGTGTCGCCAAAGAGTCATTTAATAAAATTGTAAAT
TTCTTTGATCAGAAACCAGAAGAATTGCATAACTTTTCCTTAAATTCTGAATTACATT
CTGACATAAGAAAGAACAAAATGGACATTCTAAGTTATGAGGAAACAGACATAGTT
AAACACAAAATACTGAAAGAAAGTGTCCCAGTTGGTACTGGAAATCAACTAGTGAC
CTTCCAGGGACAACCCGAACGTGATGAAAAGATCAAAGAACCTACTCTGTTGGGTT
TTCATACAGCTAGCGGGAAAAAAGTTAAAATTGCAAAGGAATCTTTGGACAAAGTG
AAAAACCTTTTTGATGAAAAAGAGCAAGGTACTAGTGAAATCACCAGTTTTAGCCAT
CAATGGGCAAAGACCCTAAAGTACAGAGAGGCCTGTAAAGACCTTGAATTAGCAT
GTGAGACCATTGAGATCACAGCTGCCCCAAAGTGTAAAGAAATGCAGAATTCTCTC
AATAATGATAAAAACCTTGTTTCTATTGAGACTGTGGTGCCACCTAAGCTCTTAAGT
GATAATTTATGTAGACAAACTGAAAATCTCAAAACATCAAAAAGTATCTTTTTGAAAG
TTAAAGTACATGAAAATGTAGAAAAAGAAACAGCAAAAAGTCCTGCAACTTGTTACA
CAAATCAGTCCCCTTATTCAGTCATTGAAAATTCAGCCTTAGCTTTTTACACAAGTT
GTAGTAGAAAAACTTCTGTGAGTCAGACTTCATTACTTGAAGCAAAAAAAATGGCTTA
GAGAAGGAATATTTGATGGTCAACCAGAAAGAATAAATACTGCAGATTATGTAGGA
AATTATTTGTATGAAAATAATTCAAACAGTACTATAGCTGAAAATGACAAAAATCATC
TCTCCGAAAAACAAGATACTTATTTAAGTAACAGTAGCATGTCTAACAGCTATTCCT
ACCATTCTGATGAGGTATATAATGATTCAGGATATCTCTCAAAAAATAAACTTGATT
CTGGTATTGAGCCAGTATTGAAGAATGTTGAAGATCAAAAAAACACTAGTTTTTCCA
AAGTAATATCCAATGTAAAAGATGCAAATGCATACCCACAAACTGTAAATGAAGATA
TTTGCGTTGAGGAACTTGTGACTAGCTCTTCACCCTGCAAAAATAAAAATGCAGCC
ATTAAATTGTCCATATCTAATAGTAATAATTTTGAGGTAGGGCCACCTGCATTTAGG
ATAGCCAGTGGTAAAATCGTTTGTGTTTCACATGAAACAATTAAAAAAGTGAAAGAC
ATATTTACAGACAGTTTCAGTAAAGTAATTAAGGAAAACAACGAGAATAAATCAAAA
ATTTGCCAAACGAAAATTATGGCAGGTTGTTACGAGGCATTGGATGATTCAGAGGA
TATTCTTCATAACTCTCTAGATAATGATGAATGTAGCACGCATTCACATAAGGTTTTT
GCTGACATTCAGAGTGAAGAAATTTTACAACATAACCAAAATATGTCTGGATTGGA
GAAAGTTTCTAAAATATCACCTTGTGATGTTAGTTTGGAAACTTCAGATATATGTAAA
TGTAGTATAGGGAAGCTTCATAAGTCAGTCTCATCTGCAAATACTTGTGGGATTTTT
AGCACAGCAAGTGGAAAATCTGTCCAGGTATCAGATGCTTCATTACAAAACGCAAG
ACAAGTGTTTTCTGAAATAGAAGATAGTACCAAGCAAGTCTTTTCCAAAGTATTGTT
TAAAAGTAACGAACATTCAGACCAGCTCACAAGAGAAGAAAATACTGCTATACGTA
CTCCAGAACATTTAATATCCCAAAAAGGCTTTTCATATAATGTGGTAAATTCATCTG

Figure 1D

CTTTCTCTGGATTTAGTACAGCAAGTGGAAAGCAAGTTTCCATTTTAGAAAGTTCCT
TACACAAAGTTAAGGGAGTGTTAGAGGAATTTGATTTAATCAGAACTGAGCATAGT
CTTCACTATTCACCTACGTCTAGACAAAATGTATCAAAAATACTTCCTCGTGTTGAT
AAGAGAAACCCAGAGCACTGTGTAAACTCAGAAATGGAAAAAACCTGCAGTAAAGA
ATTTAAATTATCAAATAACTTAAATGTTGAAGGTGGTTCTTCAGAAAATAATCACTCT
ATTAAAGTTTCTCCATATCTCTCTCAATTTCAACAAGACAAACAACAGTTGGTATTAG
GAACCAAAGTCTCACTTGTTGAGAACATTCATGTTTTGGGAAAAGAACAGGCTTCA
CCTAAAAACGTAAAAATGGAAATTGGTAAAACTGAAACTTTTTCTGATGTTCCTGTG
AAAACAAATATAGAAGTTTGTTCTACTTACTCCAAAGATTCAGAAAACTACTTTGAAA
CAGAAGCAGTAGAAATTGCTAAAGCTTTTATGGAAGATGATGAACTGACAGATTCT
AAACTGCCAAGTCATGCCACACATTCTCTTTTTACATGTCCCGAAAATGAGGAAATG
GTTTTGTCAAATTCAAGAATTGGAAAAAGAAGAGGAGAGCCCCTTATCTTAGTGGgt
aagtgttcatttttacctttcgtgttgccaatca

Exon 12
aaaacatatatgaaatatttctttttagGAGAACCCTCAATCAAAAGAAACTTATTAAATGAATTTG
ACAGGATAATAGAAAATCAAGAAAAATCCTTAAAGGCTTCAAAAAGCACTCCAGAT
Ggtaaaattagctttttatttata

Exon 13
aatatgtaatataaaataattgtttcctagGCACAATAAAAGATCGAAGATTGTTTATGCATCATGT
TTCTTTAGAGCCGATTACCTGTGTACCCTTTCGgtaagacatgtttaaatttttctaa

Exon 14
ccccattgcagCACAACTAAGGAACGTCAAGAGATACAGAATCCAAATTTTACCGCACC
TGGTCAAGAATTTCTGTCTAAATCTCATTTGTATGAACATCTGACTTTGGAAAAATCT
TCAAGCAATTTAGCAGTTTCAGGACATCCATTTTATCAAGTTTCTGCTACAAGAAAT
GAAAAAATGAGACACTTGATTACTACAGGCAGACCAACCAAAGTCTTTGTTCCACC
TTTTAAAACTAAATCaCATTTTCACAGAGTTGAACAGTGTGTTAGGAATATTAACTTG
GAGGAAAACAGACAAAAGCAAAACATTGATGGACATGGCTCTGATGATAGTAAAAA
TAAGATTAATGACAATGAGATTCATCAGTTTAACAAAAACAACTCCAATCAAGCAGC
AGCTGTAACTTTCACAAAGTGTGAAGAAGAACCTTTAGctattgtatgacaatttgtgtgatgaatt

Exon 15
tttttgctaagtatttattctttgatagATTTAATTACAAGTCTTCAGAATGCCAGAGATATACAGGAT
ATGCGAATTAAGAAGAAACAAAGGCAACGCGTCTTTCCACAGCCAGGCAGTCTGTA
TCTTGCAAAAACATCCACTCTGCCTCGAATCTCTCTGAAAGCAGCAGTAGGAGGCC
AAGTTCCCTCTGCgtgtccccataaacaggtatgtgt

Exon 16
ttttctttttttgtgtgtgtttatttttgtgtag**GTGTTCTCATAAACAG**CTGTATACGTATGGCGTTTCTAA
ACATTGCATAAAAATTAACAGCAAAAATGCAGAGTCTTTTCAGTTTCACACTGAAGA
TTATTTTGGTAAGGAAAGTTTATGGACTGGAAAAGGAATACAGTTGGCTGATGGTG
GATGGCTCATACCCTCCAATGATGGAAAGGCTGGAAAAGAAGAATTTTATAGgtactct
atgcaaaaagattgtgtgttaacttttatg

Figure 1E

Exon 17
ttatttgttcagGGCTCTGTGTGACACTCCAGGTGTGGATCCAAAGCTTATTTCTAGAATTT
GGGTTTATAATCACTATAGATGGATCATATGGAAACTGGCAGCTATGGAATGTGCC
TTTCCTAAGGAATTTGCTAATAGATGCCTAAGCCCAGAAAGGGTGCTTCTTCAACTA
AAATACAGgcaagtttaaagcatt

Exon 18
ttttgttttcacttttagATATGATACGGAAATTGATAGAAGCAGAAGATCGGCTATAAAAAAAGA
TAATGGAAAGGGATGACACAGCTGCAAAAACACTTGTTCTCTGTGTTTCTGACATA
ATTTCATTGAGCGCAAATATATCTGAAACTTCTAGCAATAAAACTAGTAGTGCAGAT
ACCCAAAAAGTGGCCATTATTGAACTTACAGATGGGTGGTATGCTGTTAAGGCCCA
GTTAGATCCTCCCCTCTTAGCTGTCTTAAAGAATGGCAGACTGACAGTTGGTCAGA
AGATTATTCTTCATGGAGCAGAACTGGTGGGCTCTCCTGATGCCTGTACACCTCTT
GAAGCCCCAGAATCTCTTATGTTAAAGgtaaatt

Exon 19
taaatcaatatatttattaatttgtccagATTTCTGCTAACAGTACTCGGCCTGCTCGCTGGTATAC
CAAACTTGGATTCTTTCCTGACCCTAGACCTTTTCCTCTGCCCTTATCATCGCTTTT
CAGTGATGGAGGAAATGTTGGTTGTGTTGATGTAATTATTCAAAGAGCATACCCTAT
ACAGgtatgatgtattcttgaaactta

Exon 20
tttggtgtgtgtaacacattattacagTGGATGGAGAAGACATCATCTGGATTATACATATTTCGC
AATGAAAGAGAGGAAGAAAAGGAAGCAGCAAAATATGTGGAGGCCCAACAAAAGA
GACTAGAAGCCTTATTCACTAAAATTCAGGAGGAATTTGAAGAACATGAAGgtaaaatt
agttatatggtacacattgttatttc

Exon 21
agtttagtgaattaataatccttttgttttcttagAAAACACAACAAAACCATATTTACCATCACGTGCAC
TAACAAGACAGCAAGTTCGTGCTTTGCAAGATGGTGCAGAGCTTTATGAAGCAGTG
AAGAATGCAGCAGACCCAGCTTACCTTGAGgtgagagagtaagaggacatataatgag

Exon 22
tttttattccaatatcttaaatggtcacagGGTTATTTCAGTGAAGAGCAGTTAAGAGCCTTGAATAA
TCACAGGCAAATGTTGAATGATAAGAAACAAGCTCAGATCCAGTTGGAAATTAGGA
AGGCCATGGAATCTGCTGAACAAAAGGAACAAGGTTTATCAAGGGATGTCACAAC
CGTGTGGAAGTTGCGTATTGTAAGCTATTCAAAAAAAGAAAAAGATTCAGgtaagtatgt
aaatgctttgttttta

Exon 23
tctccaaacagTTATACTGAGTATTTGGCGTCCATCATCAGATTTATATTCTCTGTTAACA
GAAGGAAAGAGATACAGAATTTATCATCTTGCAACTTCAAAATCTAAAAGTAAATCT
GAAAGAGCTAACATACAGTTAGCAGCGACAAAAAAAAACTCAGTATCAACAACTACC
Ggtacaaacctttcattgtaattttt

Figure 1F

Exon 24
gaatttttgttttgttttctgtagGTTTCAGATGAAATTTTATTTCAGATTTACCAGCCACGGGAGC
CCCTTCACTTCAGCAAATTTTTAGATCCAGACTTTCAGCCATCTTGTTCTGAGGTGG
ACCTAATAGGATTTGTCGTTTCTGTTGTGAAAAAAACAGgtaatgcacaatatagttaatttttttat
tgattcttttaaaaaacattgtct

Exon 25
taacattcttttctttttttttccattctagGACTTGCCCCTTTCGTCTATTTGTCAGACGAATGTTACAA
TTTACTGGCAATAAAGTTTTGGATAGACCTTAATGAGGACATTATTAAGCCTCATAT
GTTAATTGCTGCAAGCAACCTCCAGTGGCGACCAGAATCCAAATCAGGCCTTCTTA
CTTTATTTGCTGGAGATTTTTCTGTGTTTTCTGCTAGTCCAAAAGAGGGCCACTTTC
AAGAGACATTCAACAAAATGAAAAATACTGTTGAGgtaaggtta

Exon 26
ataaagcagcttttccacttattttcttagAATATTGACATACTTTGCAATGAAGCAGAAAACAAGCT
TATGCATATACTGCATGCAAATGATCCCAAGTGGTCCACCCCAACTAAAGACTGTA
CTTCAGGGCCGTACACTGCTCAAATCATTCCTGGTACAGGAAACAAGCTTCTGgtaa
gttaatgtaaactcaaggaatattataag

Exon 27
tacgttttcatttttttatcagATGTCTTCTCCTAATTGTGAGATATATTATCAAAGTCCTTTATCA
CTTTGTATGGCCAAAAGGAAGTCTGTTTCCACACCTGTCTCAGCCCAGATGACTTC
AAAGTCTTGTAAAGGGGAGAAAGAGATTGATGACCAAAAGAACTGCAAAAAGAGAA
GAGCCTTGGATTTCTTGAGTAGACTGCCTTTACCTCCACCTGTTAGTCCCATTTGTA
CATTTGTTTCTCCGGCTGCACAGAAGGCATTTCAGCCACCAAGGAGTTGTGGCAC
CAAATACGAAACACCCATAAAGAAAAAAGAACTGAATTCTCCTCAGATGACTCCATT
TAAAAAATTCAATGAAATTTCTCTTTTGGAAAGTAATTCAATAGCTGACGAAGAACTT
GCATTGATAAATACCCAAGCTCTTTTGTCTGGTTCAACAGGAGAAAAACAATTTATA
TCTGTCAGTGAATCCACTAGGACTGCTCCCACCAGTTCAGAAGATTATCTCAGACT
GAAACGACGTTGTACTACATCTCTGATCAAAGAACAGGAGAGTTCCCAGGCCAGTA
CGGAAGAATGTGAGAAAAATAAGCAGGACACAATTACAACTAAAAAATATATCTAA
GCATTTGCAAAGGCGACAATAAATTATTGACGCTTAACCTTTCCAGTTTATAAGACT
GGA

Figure 2A

Exon 2
taagtgcattttggtcttctgttttgcagACTTATTTACCAAGCATTGGAGGAATATCGTAGGTAAAA
ATGCCTATTGGATCCAAAGAGAGGCCAACATTTTTTGAAATTTTTAAGACACGCTGC
AACAAAGCAGgtattgacaaattttatataac

Exon 3
gggatttttttttaaatagATTTAGGACCAATAAGTCTTAATTGGTTTGAAGAACTTTCTTCAG
AAGCTCCACCCTATAATTCTGAACCTGCAGAAGAATCTGAACATAAAAACAACAATT
ACGAACCAAACCTATTTAAAACTCCACAAAGGAAACCATCTTATAATCAGCTGGCTT
CAACTCCAATAATATTCAAAGAGCAAGGGCTGACTCTGCCGCTGTACCAATCTCCT
GTAAAAGAATTAGATAAATTCAAATTAGACTTAGgtaagtaatgcaatatggtagactgggg

Exon 4
tcactgaattattgtactgtttcagGAAGGAATGTTCCCAATAGTAGACATAAAAGTCTTCGCACA
GTGAAAACTAAAATGGATCAAGCAGATGATGTTTCCTGTCCACTTCTAAATTCTTGT
CTTAGTGAAAGgtatgatgaagctattatattaaaa

Exon 5
agggatttgctttg**ttttattttag**TCCTGTTGTTCTACAATGTACACATGTAACACCACAAAGAG
ATAAGTCAGgtatgattaaaaacaatgctttttattctt

Exon 6
ttaacaattttccccttttttttacccccagTGGTATGTGGGAGTTTGTTTCATACACCAAAGTTTGTG
AAGgtaaatatt

Exon 7
taatgatcagggcatttctataaaaaataaactattttctttcctcccagGGTCGTCAGACACCAAAACATATT
TCTGAAAGTCTAGGAGCTGAGGTGGATCCTGATATGTCTTGGTCAAGTTCTTTAGC
TACACCACCCACCCTTAGTTCTACTGTGCTCATAGgtaataata

Exon 8
ttttatcttacagTCAGAAATGAAGAAGCATCTGAAACTGTATTTCCTCATGATACTACTGC
Tgtaagtaaatatgacattgattagact

Exon 9
taaactataatttttgcagAATGTGAAAAGCTATTTTTCCAATCATGATGAAAGTCTGAAGAAA
AATGATAGATTTATCGCTTCTGTGACAGACAGTGAAAACACAAATCAAAGAGAAGC
TGCAAGTCATGgtaagtcctct

Exon 10
ttaatgtgcttctgttttatactttaacagGATTTGGAAAAACATCAGGGAATTCATTTAAAGTAAATA
GCTGCAAAGACCACATTGGAAAGTCAATGCCAAATGTCCTAGAAGATGAAGTATAT
GAAACAGTTGTAGATACCTCTGAAGAAGATAGTTTTTCATTATGTTTTTCTAAATGTA
GAACAAAAAATCTACAAAAAGTAAGAACTAGCAAGACTAGGAAAAAAATTTTCCATG
AAGCAAACGCTGATGAATGTGAAAAATCTAAAAACCAAGTGAAAGAAAAATACTCAT
TTGTATCTGAAGTGGAACCAAATGATACTGATCCATTAGATTCAAATGTAGCAAATC

Figure 2B

AGAAGCCCTTTGAGAGTGGAAGTGACAAAATCTCCAAGGAAGTTGTACCGTCTTTG
GCCTGTGAATGGTCTCAACTAACCCTTTCAGGTCTAAATGGAGCCCAGATGGAGAA
AATACCCCTATTGCATATTTCTTCATGTGACCAAAATATTTCAGAAAAAGACCTATTA
GACACAGAGAACAAAAGAAAGAAAGATTTTCTTACTTCAGAGAATTCTTTGCCACGT
ATTTCTAGCCTACCAAAATCAGAGAAGCCATTAAATGAGGAAACAGTGGTAAATAA
GAGAGATGAAGAGCAGCATCTTGAATCTCATACAGACTGCATTCTTGCAGTAAAGC
AGGCAATATCTGGAACTTCTCCAGTGGCTTCTTCATTTCAGGGTATCAAAAAGTCTA
TATTCAGAATAAGAGAATCACCTAAAGAGACTTTCAATGCAAGTTTTTCAGGTCATA
TGACTGATCCAAACTTTAAAAAAGAAACTGAAGCCTCTGAAAGTGGACTGGAAATA
CATACTGTTTGCTCACAGAAGGAGGACTCCTTATGTCCAAATTTAATTGATAATGGA
AGCTGGCCAGCCACCACCACACAGAATTCTGTAGCTTTGAAGAATGCAGGTTTAAT
ATCCACTTTGAAAAAGAAAACAAATAAGTTTATTTATGCTATACATGATGAAACATCT
TATAAAGGAAAAAAAAATACCGAAAGACCAAAAATCAGAACTAATTAACTGTTCAGCC
CAGTTTGAAGCAAATGCTTTTGAAGCACCACTTACATTTGCAAATGCTGATTCAGGt
acctctgtct

Exon 11

tttgtgtttttatgtttagGTTTATTGCATTCTTCTGTGAAAAGAAGCTGTTCACAGAATGATTCT
GAAGAACCAACTTTGTCCTTAACTAGCTCTTTTGGGACAATTCTGAGGAAATGTTCT
AGAAATGAAACATGTTCTAATAATACAGTAATCTCTCAGGATCTTGATTATAAAGAA
GCAAAATGTAATAAGGAAAAACTACAGTTATTTATTACCCCAGAAGCTGATTCTCTG
TCATGCCTGCAGGAAGGACAGTGTGAAAATGATCCAAAAAGCAAAAAAGTTTCAGA
TATAAAAGAAGAGGTCTTGGCTGCAGCATGTCACCCAGTACAACATTCAAAAGTGG
AATACAGTGATACTGACTTTCAATCCCAGAAAAGTCTTTTATATGATCATGAAAATG
CCAGCACTCTTATTTTAACTCCTACTTCCAAGGATGTTCTGTCAAACCTAGTCATGA
TTTCTAGAGGCAAAGAATCATACAAAATGTCAGACAAGCTCAAAGGTAACAATTATG
AATCTGATGTTGAATTAACCAAAAATATTCCCATGGAAAAGAATCAAGATGTATGTG
CTTTAAATGAAAATTATAAAAACGTTGAGCTGTTGCCACCTGAAAAATACATGAGAG
TAGCATCACCTTCAAGAAAGGTACAATTCAACCAAAACACAAATCTAAGAGTAATCC
AAAAAAATCAAGAAGAAACTACTTCAATTTCAAAAATAACTGTCAATCCAGACTCTG
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ATAATCTTGCTTTAGGAAATACTAAGGAACTTCATGAAACAGACTTGACTTGTGTAA
ACGAACCCATTTTCAAGAACTCTACCATGGTTTTATATGGAGACACAGGTGATAAAC
AAGCAACCCAAGTGTCAATTAAAAAAGATTTGGTTTATGTTCTTGCAGAGGAGAAC
AAAAATAGTGTAAAGCAGCATATAAAAATGACTCTAGGTCAAGATTTAAAATCGGAC
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GCAGGACTCTTAGGTCCAATTTCAAATCACAGTTTTGGAGGTAGCTTCAGAACAGC
TTCAAATAAGGAAATCAAGCTCTCTGAACATAACATTAAGAAGAGCAAAATGTTCTT
CAAAGATATTGAAGAACAATATCCTACTAGTTTAGCTTGTGTTGAAATTGTAAATAC
CTTGGCATTAGATAATCAAAAGAAACTGAGCAAGCCTCAGTCAATTAATACTGTATC
TGCACATTTACAGAGTAGTGTAGTTGTTTCTGATTGTAAAAATAGTCATATAACCCC
TCAGATGTTATTTTCCAAGCAGGATTTTAATTCAAACCATAATTTAACACCTAGCCAA
AAGGCAGAAATTACAGAACTTTCTACTATATTAGAAGAATCAGGAAGTCAGTTTGAA
TTTACTCAGTTTAGAAAACCAAGCTACATATTGCAGAAGAGTACATTTGAAGTGCCT
GAAAACCAGATGACTATCTTAAAGACCACTTCTGAGGAATGCAGAGATGCTGATCT
TCATGTCATAATGAATGCCCCATCGATTGGTCAGGTAGACAGCAGCAAGCAATTTG

Figure 2C

AAGGTACAGTTGAAATTAAACGGAAGTTTGCTGGCCTGTTGAAAAATGACTGTAAC
AAAAGTGCTTCTGGTTATTTAACAGATGAAAATGAAGTGGGGTTTAGGGGCTTTTAT
TCTGCTCATGGCACAAAACTGAATGTTTCTACTGAAGCTCTGCAAAAAGCTGTGAA
ACTGTTTAGTGATATTGAGAATATTAGTGAGGAAACTTCTGCAGAGGTACATCCAAT
AAGTTTATCTTCAAGTAAATGTCATGATTCTGTTGTTTCAATGTTTAAGATAGAAAAT
CATAATGATAAAACTGTAAGTGAAAAAAATAATAAATGCCAACTGATATTACAAAATA
ATATTGAAATGACTACTGGCACTTTTGTTGAAGAAATTACTGAAAATTACAAGAGAA
ATACTGAAAATGAAGATAACAAATATACTGCTGCCAGTAGAAATTCTCATAACTTAG
AATTTGATGGCAGTGATTCAAGTAAAAATGATACTGTTTGTATTCATAAAGATGAAA
CGGACTTGCTATTTACTGATCAGCACAACATATGTCTTAAATTATCTGGCCAGTTTA
TGAAGGAGGGAAACACTCAGATTAAAGAAGATTTGTCAGATTTAACTTTTTTGGAAG
TTGCGAAAGCTCAAGAAGCATGTCATGGTAATACTTCAAATAAAGAACAGTTAACT
GCTACTAAAACGGAGCAAAATATAAAAGATTTTGAGACTTCTGATACATTTTTTCAG
ACTGCAAGTGGGAAAAATATTAGTGTCGCCAAAGAGTCATTTAATAAAATTGTAAAT
TTCTTTGATCAGAAACCAGAAGAATTGCATAACTTTTCCTTAAATTCTGAATTACATT
CTGACATAAGAAAGAACAAAATGGACATTCTAAGTTATGAGGAAACAGACATAGTT
AAACACAAAATACTGAAAGAAAGTGTCCCAGTTGGTACTGGAAATCAACTAGTGAC
CTTCCAGGGACAACCCGAACGTGATGAAAAGATCAAAGAACCTACTCTGTTGGGTT
TTCATACAGCTAGCGGGAAAAAAGTTAAAATTGCAAAGGAATCTTTGGACAAAGTG
AAAAACCTTTTTGATGAAAAAGAGCAAGGTACTAGTGAAATCACCAGTTTTAGCCAT
CAATGGGCAAAGACCCTAAAGTACAGAGAGGCCTGTAAAGACCTTGAATTAGCAT
GTGAGACCATTGAGATCACAGCTGCCCCAAAGTGTAAAGAAATGCAGAATTCTCTC
AATAATGATAAAAACCTTGTTTCTATTGAGACTGTGGTGCCACCTAAGCTCTTAAGT
GATAATTTATGTAGACAAACTGAAAATCTCAAAACATCAAAAAGTATCTTTTTGAAAG
TTAAAGTACATGAAAATGTAGAAAAAGAAACAGCAAAAAGTCCTGCAACTTGTTACA
CAAATCAGTCCCCTTATTCAGTCATTGAAAATTCAGCCTTAGCTTTTTACACAAGTT
GTAGTAGAAAAACTTCTGTGAGTCAGACTTCATTACTTGAAGCAAAAAAATGGCTTA
GAGAAGGAATATTTGATGGTCAACCAGAAAGAATAAATACTGCAGATTATGTAGGA
AATTATTTGTATGAAAATAATTCAAACAGTACTATAGCTGAAAATGACAAAAATCATC
TCTCCGAAAAACAAGATACTTATTTAAGTAACAGTAGCATGTCTAACAGCTATTCCT
ACCATTCTGATGAGGTATATAATGATTCAGGATATCTCTCAAAAAATAAACTTGATT
CTGGTATTGAGCCAGTATTGAAGAATGTTGAAGATCAAAAAAACACTAGTTTTTCCA
AAGTAATATCCAATGTAAAAGATGCAAATGCATACCCACAAACTGTAAATGAAGATA
TTTGCGTTGAGGAACTTGTGACTAGCTCTTCACCCTGCAAAAATAAAAATGCAGCC
ATTAAATTGTCCATATCTAATAGTAATAATTTTGAGGTAGGGCCACCTGCATTTAGG
ATAGCCAGTGGTAAAATC**GTTTGTGTT**TCACATGAAACAATTAAAAAAGTGAAAGAC
ATATTTACAGACAGTTTCAGTAAAGTAATTAAGGAAAACAACGAGAATAAATCAAAA
ATTTGCCAAACGAAAATTATGGCAGGTTGTTACGAGGCATTGGATGATTCAGAGGA
TATTCTTCATAACTCTCTAGATAATGATGAATGTAGCACGCATTCACATAAGGTTTTT
GCTGACATTCAGAGTGAAGAAATTTTACAACATAACCAAAATATGTCTGGATTGGA
GAAAGTTTCTAAAATATCACCTTGTGATGTTAGTTTGGAAACTTCAGATATATGTAAA
TGTAGTATAGGGAAGCTTCATAAGTCAGTCTCATCTGCAAATACTTGTGGGATTTTT
AGCACAGCAAGTGGAAAATCTGTCCAGGTATCAGATGCTTCATTACAAAACGCAAG
ACAAGTGTTTTCTGAAATAGAAGATAGTACCAAGCAAGTCTTTTCCAAAGTATTGTT
TAAAAGTAACGAACATTCAGACCAGCTCACAAGAGAAGAAAATACTGCTATACGTA
CTCCAGAACATTTAATATCCCAAAAAGGCTTTTCATATAATGTGGTAAATTCATCTG

Figure 2D

CTTTCTCTGGATTTAGTACAGCAAGTGGAAAGCAAGTTTCCATTTTAGAAAGTTCCT
TACACAAAGTTAAGGGAGTGTTAGAGGAATTTGATTTAATCAGAACTGAGCATAGT
CTTCACTATTCACCTACGTCTAGACAAAATGTATCAAAAATACTTCCTCGTGTTGAT
AAGAGAAACCCAGAGCACTGTGTAAACTCAGAAATGGAAAAAACCTGCAGTAAAGA
ATTTAAATTATCAAATAACTTAAATGTTGAAGGTGGTTCTTCAGAAAATAATCACTCT
ATTAAAGTTTCTCCATATCTCTCTCAATTTCAACAAGACAAACAACAGTTGGTATTAG
GAACCAAAGTCTCACTTGTTGAGAACATTCATGTTTTGGGAAAAGAACAGGCTTCA
CCTAAAAACGTAAAAATGGAAATTGGTAAAACTGAAACTTTTTCTGATGTTCCTGTG
AAAACAAATATAGAAGTTTGTTCTACTTACTCCAAAGATTCAGAAAACTACTTTGAAA
CAGAAGCAGTAGAAATTGCTAAAGCTTTTATGGAAGATGATGAACTGACAGATTCT
AAACTGCCAAGTCATGCCACACATTCTCTTTTTACATGTCCCGAAAATGAGGAAATG
GTTTTGTCAAATTCAAGAATTGGAAAAAGAAGAGGAGAGCCCCTTATCTTAGTGGgt
aagtgttcatttttacctttcgtgttgccaatca

Exon 12
aaaacatatatgaaatatttctttttagGAGAACCCTCAATCAAAAGAAACTTATTAAATGAATTTG
ACAGGATAATAGAAAATCAAGAAAAATCCTTAAAGGCTTCAAAAAGCACTCCAGAT
Ggtaaaattagctttttatttata

Exon 13
aatatgtaatataaaataattgtttcctagGCACAATAAAAGATCGAAGATTGTTTATGCATCATGT
TTCTTTAGAGCCGATTACCTGTGTACCCTTTCGgtaagacatgtttaaatttttctaa

Exon 14
ccccattgcagCACAACTAAGGAACGTCAAGAGATACAGAATCCAAATTTTACCGCACC
TGGTCAAGAATTTCTGTCTAAATCTCATTTGTATGAACATCTGACTTTGGAAAAATCT
TCAAGCAATTTAGCAGTTTCAGGACATCCATTTTATCAAGTTTCTGCTACAAGAAAT
GAAAAAATGAGACACTTGATTACTACAGGCAGACCAACCAAAGTCTTTGTTCCACC
TTTTAAAACTAAATCACATTTTCACAGAGTTGAACAGTGTGTTAGGAATATTAACTTG
GAGGAAAACAGACAAAAGCAAAACATTGATGGACATGGCTCTGATGATAGTAAAAA
TAAGATTAATGACAATGAGATTCATCAGTTTAACAAAAACAACTCCAATCAAGCAGC
AGCTGTAACTTTCACAAAGTGTGAAGAAGAACCTTTAGgtattgtatgacaatttgtgtgatgaatt

Exon 15
tttttgctaagtatttattctttgatagATTTAATTACAAGTCTTCAGAATGCCAGAGATATACAGGAT
ATGCGAATTAAGAAGAAACAAAGGCAACGCGTCTTTCCACAGCCAGGCAGTCTGTA
TCTTGCAAAAACATCCACTCTGCCTCGAATCTCTCTGAAAGCAGCAGTAGGAGGCC
AAGTTCCCTCTGC**GTGTTCTCATAAACAG**gtatgtgt

Exon 16
ttttctttttgtgtgtgtttattttgtgtagCTGTATACGTATGGCGTTTCTAAACATTGCATAAAAATTA
ACAGCAAAAATGCAGAGTCTTTTCAGTTTCACACTGAAGATTATTTTGGTAAGGAAA
GTTTATGGACTGGAAAAGGAATACAGTTGGCTGATGGTGGATGGCTCATACCCTCC
AATGATGGAAAGGCTGGAAAAGAAGAATTTTATAGgtactctatgcaaaaagattgtgtgttaacttttt
atg

Figure 2E

Exon 17

ttatttgttcagGGCTCTGTGTGACACTCCAGGTGTGGATCCAAAGCTTATTTCTAGAATTT
GGGTTTATAATCACTATAGATGGATCATATGGAAACTGGCAGCTATGGAATGTGCC
TTTCCTAAGGAATTTGCTAATAGATGCCTAAGCCCAGAAAGGGTGCTTCTTCAACTA
AAATACAGgcaagtttaaagcatt

Exon 18

ttttgttttcacttttagATATGATACGGAAATTGATAGAAGCAGAAGATCGGCTATAAAAAAAGA
TAATGGAAAGGGATGACACAGCTGCAAAAACACTTGTTCTCTGTGTTTCTGACATA
ATTTCATTGAGCGCAAATATATCTGAAACTTCTAGCAATAAAACTAGTAGTGCAGAT
ACCCAAAAAGTGGCCATTATTGAACTTACAGATGGGTGGTATGCTGTTAAGGCCCA
GTTAGATCCTCCCCTCTTAGCTGTCTTAAAGAATGGCAGACTGACAGTTGGTCAGA
AGATTATTCTTCATGGAGCAGAACTGGTGGGCTCTCCTGATGCCTGTACACCTCTT
GAAGCCCCAGAATCTCTTATGTTAAAGgtaaatt

Exon 19

taaatcaatatatttattaatttgtccagATTTCTGCTAACAGTACTCGGCCTGCTCGCTGGTATAC
CAAACTTGGATTCTTTCCTGACCCTAGACCTTTTCCTCTGCCCTTATCATCGCTTTT
CAGTGATGGAGGAAATGTTGGTTGTGTTGATGTAATTATTCAAAGAGCATACCCTAT
ACAGgtatgatgtattcttgaaactta

Exon 20

tttggtgtgtgtaacacattattacagTGGATGGAGAAGACATCATCTGGATTATACATATTTCGC
AATGAAAGAGAGGAAGAAAAGGAAGCAGCAAAATATGTGGAGGCCCAACAAAAGA
GACTAGAAGCCTTATTCACTAAAATTCAGGAGGAATTTGAAGAACATGAAGgtaaaatt
agttatatggtacacattgttatttc

Exon 21

agtttagtgaattaataatccttttgttttcttagAAAACACAACAAAACCATATTTACCATCACGTGCAC
TAACAAGACAGCAAGTTCGTGCTTTGCAAGATGGTGCAGAGCTTTATGAAGCAGTG
AAGAATGCAGCAGACCCAGCTTACCTTGAGgtgagagagtaagaggacatataatgag

Exon 22

tttttattccaatatcttaaatggtcacagGGTTATTTCAGTGAAGAGCAGTTAAGAGCCTTGAATAA
TCACAGGCAAATGTTGAATGATAAGAAACAAGCTCAGATCCAGTTGGAAATTAGGA
AGgCCATGGAATCTGCTGAACAAAAGGAACAAGGTTTATCAAGGGATGTCACAACC
GTGTGGAAGTTGCGTATTGTAAGCTATTCAAAAAAAGAAAAAGATTCAGgtaagtatgta
aatgctttgttttta

Exon 23

tctccaaacagTTATACTGAGTATTTGGCGTCCATCATCAGATTTATATTCTCTGTTAACA
GAAGGAAAGAGATACAGAATTTATCATCTTGCAACTTCAAAATCTAAAAGTAAATCT
GAAAGAGCTAACATACAGTTAGCAGCGACAAAAAAAAACTCAGTATCAACAACTACC
Ggtacaaaacctttcattgtaattttt

Figure 2F

Exon 24

gaatttttgttttgttttctgtagGTTTCAGATGAAATTTTATTTCAGATTTACCAGCCACGGGAGC
CCCTTCACTTCAGCAAATTTTTAGATCCAGACTTTCAGCCATCTTGTTCTGAGGTGG
ACCTAATAGGATTTGTCGTTTCTGTTGTGAAAAAAACAGgtaatgcacaatatagttaatttttttat
tgattcttttaaaaaacattgtct

Exon 25

taacattcttttctttttttttccattctagGACTTGCCCCTTTCGTCTATTTGTCAGACGAATGTTACAA
TTTACTGGCAATAAAGTTTTGGATAGACCTTAATGAGGACATTATTAAGCCTCATAT
GTTAATTGCTGCAAGCAACCTCCAGTGGCGACCAGAATCCAAATCAGGCCTTCTTA
CTTTATTTGCTGGAGATTTTTCTGTGTTTTCTGCTAGTCCAAAAGAGGGCCACTTTC
AAGAGACATTCAACAAAATGAAAAATACTGTTGAGgtaaggtta

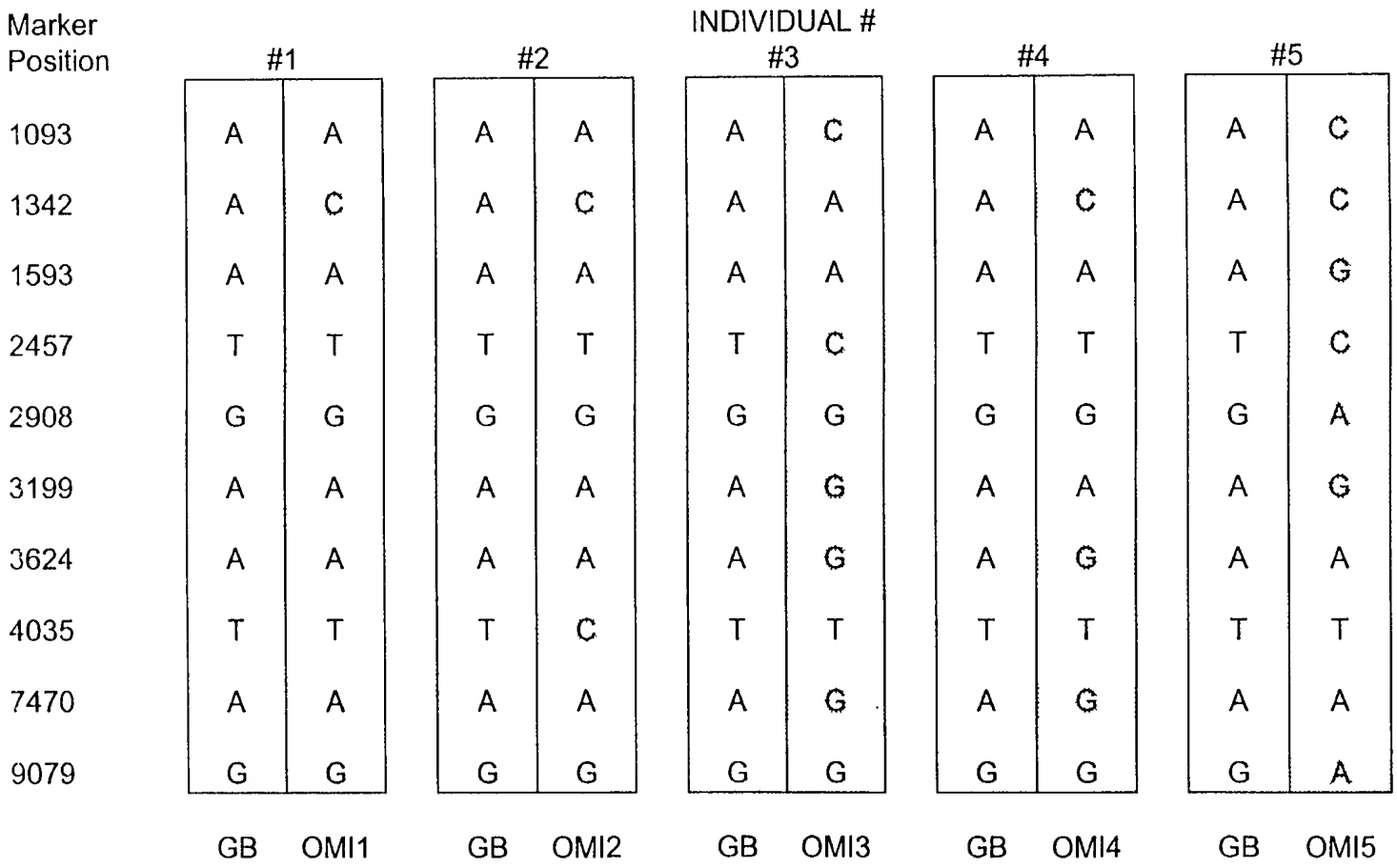
Exon 26

ataaagcagcttttccacttattttcttagAATATTGACATACTTTGCAATGAAGCAGAAAACAAGCT
TATGCATATACTGCATGCAAATGATCCCAAGTGGTCCACCCCAACTAAAGACTGTA
CTTCAGGGCCGTACACTGCTCAAATCATTCCTGGTACAGGAAACAAGCTTCTGgtaa
gttaatgtaaactcaaggaatattataag

Exon 27

tacgttttcatttttttatcagATGTCTTCTCCTAATTGTGAGATATATTATCAAAGTCCTTTATCA
CTTTGTATGGCCAAAAGGAAGTCTGTTTCCACACCTGTCTCAGCCCAGATGACTTC
AAAGTCTTGTAAAGGGGAGAAAGAGATTGATGACCAAAAGAACTGCAAAAAGAGAA
GAGCCTTGGATTTCTTGAGTAGACTGCCTTTACCTCCACCTGTTAGTCCCATTTGTA
CATTTGTTTCTCCGGCTGCACAGAAGGCATTTCAGCCACCAAGGAGTTGTGGCAC
CAAATACGAAACACCCATAAAGAAAAAAGAACTGAATTCTCCTCAGATGACTCCATT
TAAAAAATTCAATGAAATTTCTCTTTTGGAAAGTAATTCAATAGCTGACGAAGAACTT
GCATTGATAAATACCCAAGCTCTTTTGTCTGGTTCAACAGGAGAAAAACAATTTATA
TCTGTCAGTGAATCCACTAGGACTGCTCCCACCAGTTCAGAAGATTATCTCAGACT
GAAACGACGTTGTACTACATCTCTGATCAAAGAACAGGAGAGTTCCCAGGCCAGTA
CGGAAGAATGTGAGAAAAATAAGCAGGACACAATTACAACTAAAAAATATATCTAA
GCATTTGCAAAGGCGACAATAAATTATTGACGCTTAACCTTTCCAGTTTATAAGACT
GGA

FIGURE 3



VERIFIED STATEMENT CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) & 1.27(c)) - SMALL BUSINESS CONCERN	Docket No: 05371.31.US02 PA-

Applicant or Patentee: Patricia D. Murphy; Marga B. White; Mark B. Rabin; Sheri J. Olson; Matthew Yoshikawa; Geoffrey M. Jackson; Tara Eskandari; Brenda Schryer; and Michael Park.
Serial or Patent No.: To be assigned.
Filed or Issued: Herewith
Title: NOVEL CODING SEQUENCE HAPLOTYPES OF THE HUMAN BRCA2 GENE

I hereby declare that I am

___ the owner of the small business concern identified below:
XXX an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF SMALL BUSINESS CONCERN: Oncormed, Inc.
ADDRESS OF SMALL BUSINESS CONCERN: 205 Perry Parkway
Gaithersburg, MD 20877

I hereby declare that the above-identified small business concern qualifies as a small business concern as defined in 13 CFR 121.12, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees to the United States Patent and Trademark Office, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the pervious fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls of has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention described in:

XXXX the specification filed herewith with title as listed above.
_____ the application identified above.
_____ the patent identified above.

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights in the invention must file separate verified statements averring to their status as small entities, and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d), or a nonprofit organization under 37 CFR 1.9(e).

_____ Each person, concern or organization having any rights in the invention is listed below.
XXX No such person, concern or organization exists.
_____ Each such person, concern or organization is listed below.

Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fees due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b)).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, and patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING: DOUG DOLGINOW, M.D.
TITLE OF PERSON IF OTHER THAN OWNER: President & C.O.O.
ADDRESS OF PERSON SIGNING: 205 Perry Parkway
Gaithersburg, MD 20877

SIGNATURE _____ DATE 5/13/98

JCR SED

Combined Declaration and Power of Attorney for Patent Application

Docket Number: **5371.31.US02**

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am an original, first and joint inventor (if plural names are listed below) of the subject matter that is claimed and for which a patent is sought on the invention entitled **NOVEL CODING SEQUENCE HAPLOTYPES OF THE HUMAN BRCA2 GENE**, the specification of which is attached hereto unless the following box is checked:

■ was filed on **Herewith**;
as United States Application Number or PCT International Application Number **To Be Assigned**; and
was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information that is material to patentability as defined in 37 C.F.R. § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application, which designated at least one country other than the United States listed below, and have also identified below any foreign application for patent or inventor's certificate, or PCT international application having a filing date before that of the application on which priority is claimed.

PRIOR FOREIGN APPLICATION(S)			
Application No.	**Country**	**(Day/Month/Year/Filed)**	**Priority Claimed**
			Yes No
			Yes No
			Yes No
			Yes No

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below.

Application No.	Filing Date
60/055,784	August 15, 1997
60/064,926	November 7, 1997
60/065,367	November 12, 1997

I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s), or under § 365(c) of any PCT international application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose information that is material to patentability as defined in 37 C.F.R. § 1.56 that became available between the filing date of the prior application and the national or PCT international filing date of this application.

Application No.	Filing Date	(Status – patented, pending, abandoned)

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Jeffrey I. Auerbach, Reg. No. 32,680
Melvin L. Barnes, Jr. Reg. No. 38,375
Thane Bauz, Reg. No. P41,604
Michael J. Bell, Reg. No. 39,604
John A. Bendrick, Reg. No. P41,612
Mark R. Buscher, Reg. No. 35,006
Celine T. Callahan, Reg. No. 34,301
Cono A. Carrano, Reg. No. 39,623
James F. Davis, Reg. No. 21,072
Thomas M. Dunham, Reg. No. 39,965
Joel M. Freed, Reg. No. 25,101
Vernon Randall Gard, Reg. No. 33,886
Alan M. Grimaldi, Reg. No. 26,599
Alexander J. Hadjis, Reg. No. 36,540
Albert P. Halluin, Reg. No. 25,227
Michael N. Haynes, Reg. No. 40,014
Rouget F. Henschel, Reg. No. 39,221
Leslie L. Jacobs, Jr., Reg. No. 40,659
Richard H. Kjeldgaard, Reg. No. 30,186
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Kevin W. McCabe, Reg. No. 41,182
Joseph A. Micallef, Reg. No. 39,772
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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

FULL NAME OF SOLE OR FIRST INVENTOR: Patricia D. Murphy	**CITIZENSHIP:** USA
RESIDENCE: Slingerlands, New York, USA	**DATE:** 5/8/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Patricia D Murphy
FULL NAME OF SECOND INVENTOR: Marga B. White	**CITIZENSHIP:** USA
RESIDENCE: Frederick, Maryland, USA	**DATE:** 5/13/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Marga B White
FULL NAME OF THIRD INVENTOR: Mark B. Rabin	**CITIZENSHIP:** USA
RESIDENCE: Rockville, Maryland, USA	**DATE:** 5/13/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Mark Rabin

(Supply similar information and signature for subsequent joint inventors, if any)

FULL NAME OF FOURTH INVENTOR: Sheri J. Olson	**CITIZENSHIP:** USA
RESIDENCE: Falls Church, Virginia, USA	**DATE:** 5/13/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Sheri J. Olson
FULL NAME OF FIFTH INVENTOR: Matthew Yoshikawa	**CITIZENSHIP:** USA
RESIDENCE ADDRESS: Germantown, Maryland, USA	**DATE:**
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:**
FULL NAME OF SIXTH INVENTOR: Geoffrey M. Jackson	**CITIZENSHIP:** USA
RESIDENCE ADDRESS: Beltsville, Maryland, USA	**DATE:**
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:**
FULL NAME OF SEVENTH INVENTOR: Tara Eskandari	**CITIZENSHIP:** USA
RESIDENCE ADDRESS: Rockville, Maryland, USA	**DATE:** 5-13-98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Tara Eskandari
FULL NAME OF EIGHTH INVENTOR: Brenda Schryer	**CITIZENSHIP:** USA
RESIDENCE ADDRESS: Bel Air, Maryland, USA	**DATE:** 5-16-98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Brenda Schryer
FULL NAME OF NINTH INVENTOR: Michael Park	**CITIZENSHIP:** USA
RESIDENCE ADDRESS: Rockville, Maryland, USA	**DATE:** 5/13/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Michael H. Park

(Supply similar information and signature for subsequent joint inventors, if any)

Combined Declaration and Power of Attorney for Patent Application

Docket Number: **5371.31.US02**

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am an original, first and joint inventor (if plural names are listed below) of the subject matter that is claimed and for which a patent is sought on the invention entitled **NOVEL CODING SEQUENCE HAPLOTYPES OF THE HUMAN BRCA2 GENE**, the specification of which is attached hereto unless the following box is checked:

■ was filed on **Herewith** ;
as United States Application Number or PCT International Application Number **To Be Assigned** ; and
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I acknowledge the duty to disclose information that is material to patentability as defined in 37 C.F.R. § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application, which designated at least one country other than the United States listed below, and have also identified below any foreign application for patent or inventor's certificate, or PCT international application having a filing date before that of the application on which priority is claimed.

PRIOR FOREIGN APPLICATION(S)			
Application No.	**Country**	**(Day/Month/Year/Filed)**	**Priority Claimed**
			Yes No
			Yes No
			Yes No
			Yes No

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below.

Application No.	Filing Date
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FULL NAME OF SECOND INVENTOR: Marga B. White	**CITIZENSHIP:** USA
RESIDENCE: Frederick, Maryland, USA	**DATE:** 5/13/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Marga Bich White
FULL NAME OF THIRD INVENTOR: Mark B. Rabin	**CITIZENSHIP:** USA
RESIDENCE: Rockville, Maryland, USA	**DATE:** 5/13/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Mark Rabin

(Supply similar information and signature for subsequent joint inventors, if any)

FULL NAME OF FOURTH INVENTOR: Sheri J. Olson	**CITIZENSHIP:** USA
RESIDENCE: Falls Church, Virginia, USA	**DATE:** 5/13/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Sheri J. Olson
FULL NAME OF FIFTH INVENTOR: Matthew Yoshikawa	**CITIZENSHIP:** USA
RESIDENCE ADDRESS: Germantown, Maryland, USA	**DATE:** 5/13/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:**
FULL NAME OF SIXTH INVENTOR: Geoffrey M. Jackson	**CITIZENSHIP:** USA
RESIDENCE ADDRESS: Beltsville, Maryland, USA	**DATE:** 5/15/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** G. M. Jackson
FULL NAME OF SEVENTH INVENTOR: Tara Eskandari	**CITIZENSHIP:** USA
RESIDENCE ADDRESS: Rockville, Maryland, USA	**DATE:** 5-13-98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** T. Eskandari
FULL NAME OF EIGHTH INVENTOR: Brenda Schryer	**CITIZENSHIP:** USA
RESIDENCE ADDRESS: Bel Air, Maryland, USA	**DATE:**
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:**
FULL NAME OF NINTH INVENTOR: Michael Park	**CITIZENSHIP:** USA
RESIDENCE ADDRESS: Rockville, Maryland, USA	**DATE:** 5/13/98
POST OFFICE ADDRESS: 205 Perry Parkway, Gaithersburg, Maryland 20877, USA	**INVENTOR'S SIGNATURE:** Michael J. Park

(Supply similar information and signature for subsequent joint inventors, if any)